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FIG.1

GGATCCCTGCTCCAGCAGCTGCAAGGTGCAAGAAGAAGAAGATCCCAGGGAGGAAAAATGTG	120
CTGGAGACCCCTGTGTGGGTTCTGTGGCTTTGGTCCTATCTGTCTTATGTTCAAGCAGT	180
W R P L C R F L W L W S Y L S Y V Q A V	22
GCCTATCCAAAAAGTCCAGGATGACACCAAAACCCTCATCAAGACCATTGTCACCAGGAT	240
P I Q K V Q D D T K T L I K T I V T R I	42
CAATGACATTTTACACACGGCASTCGGTATCCGCCAAGCAGAGGGTCACTGGCTTGGACTT	300
N D I S H T Q S V S A K Q R V T G L D F	62
CATTCTCTGGGCTTCAACCCATTCTGAGTTTGTCCAAGATGGACCAGACTCTGGCACTCTA	360
I P G L H P I L S L S K M D Q T L A V Y	82
TCAACAGGTCTCTACCAGCCTGCCTTCCCAAAATGTGCTGCAGATAGCCAATGACCTGGA	420
Q Q V L T S L P S Q N V L Q I A N D L E	102
GAATCTCCGAGACCTCCTCCATCTGCTGGCCTTCTCCAAGAGCTGCTCCCTGCCTCAGAC	480
N L R D L L H L L A F S K S C S L P Q T	122
CAGTGGCCTGCAGAAGCCAGAGAGCCTGGATGGCGTCTGGAAGCCTCACTCTACTCCAC	540
S G L Q K P E S L D G V L E A S L Y S T	142
AGAGGTGGTGGCTTTGAGCAGGCTGCAGGGCTCTCTGCAGGACATTCTTCAACAGTTGGA	600
E V V A L S R L Q G S L Q D I L Q Q L D	162
TGTTAGCCCTGAATGCTGAAGTTTCAAAGGCCACCAGGCTCCCAAGAATCATGTAGAGGG	660
V S P E C *	167
AAGAAACCTTGGCTTCCAGGGGTCTTCAGGAGAAGAGAGCCATGTGCACACATCCATCAT	720
TCATTTCTCTCCCTCCTGTAGACCACCCATCCAAAGGCATGACTCCACAATGCTTGACTC	780
AAGTTATCCACACAACCTTCATGAGCACAAGGAGGGGCCAGCCTGCAGAGGGGACTCTCAC	840
CTAGTTCTTCAGCAAGTAGAGATAAGAGCCATCCCATCCCCTCCATGTCCCACCTGCTCC	900
GGGTACATGTTCTCCTCCGTGGGTACACGCTTCGCTGCGGGCCAGGAGAGGTGAGGTAGGGA	960
TGGGTAGAGCCTTTGGGCTGTCTCAGAGTCTTTGGGAGCACCGTGAAGGCTGCATCCACA	1020
CACAGCTGGAACCTCCCAAGCAGCACACGATGGAAGCACTTATTTATTTATTCTGCATTC	1080
TATTTTGGATGGATCTGAAGCAAGGCATCAGCTTTTTTTCAGGCTTTGGGGGTTCAGCCAGGA	1140
TGAGGAAGGCTCCTGGGGTGTCTGCTTTCAATCCTATTGATGGGTCTGCCCCAGGCCAAACC	1200
TAATTTTGTAGTGAAGGCAAGGTTGGGATCTTCCAAACAAGAGTCTATGCAGGTAG	1260
CGCTCAAGATTGACCTCTGGTGAAGTGGTGTGTTTCTATTGTGACTGACTCTATCCAAAC	1320
ACGTTTGCAGCGGCATTGCCGGGAGCATAGGCTAGGTTATTATCAAAAGCAGATGAATTT	1380
TGTCAAGTGTAATATGTATCTATGTGCACCTGAGGGTAGAGGATGTGTTAGAGGGAGGGT	1440
GAAGGATCCCGAAGTGTTCTCTGAATTACATATGTGTGGTAGGCTTTTCTGAAAGGGTGA	1500
GGCATTTTCTTACCTCTGTGGCCACATAGTGTGGCTTTGTGAAAAGGACAAAGGAGTTGA	1560
CTCTTTCCGGAACATTTGGAGTGTACCAGGCACCTTGGAGGGGGCTAAAGCTACAGGCCCT	1620
TTTGTGGCATATTGCTGAGCTCAGGGAGTGAGGGCCCCACATTTGAGACAGTGAGCCCC	1680
AAGAAAAGGGTCCCTGGTGTAGATCTCCAAGGTTGTCCAGGGTTGATCTCACAATGCGTT	1740
TCTTAAGCAGGTAGACGTTTGCATGCCAATATGTGGTTCTCATCTGATTGGTTTATCCAA	1800
AGTAGAACCTGTCTCCACCCATTCTGTGGGGAGTTTGTGTTCCAGTGAGGAATGAGAAAT	1860
CACCTAGCAGATGGTCTTGAGCCCTGGGGCCAGCAGTGTGAGGAAGTGCCAGGGCCCCAG	1920
GCCAGGCTGCCAGAAATTGCCCTTCGGGCTGGAGGATGAACAAAGGGGCTTGGGTTTTTCC	1980
ATCACCCCTGCACCCATGTACCATCAAACCTGGGGGGCAGATCAGTGAGAGGACACTTG	2040
ATGGAAAGCAATACACTTTAAGACTGAGCACAGTTTCGTGCTCAGCTCTGTCTGGTGTCTG	2100
TGAGCTAGAGAAGCTCACCACATACATATAAAATCAGAGGCTCATGTCCCTGTGGTTAG	2160
ACCCTACTCGCGGCGGTGTACTCCACCACAGCAGCACCGCACCGCTGGAAGTACAGTGCT	2220
GTCTTCAACAGGTGTGAAAGAACCTGAGCTGAGGGTGACAGTGCCAGGGGAACCTGTCT	2280
TGCAGTCTATTGCATTTACATACCGCATTTTCAGGGCACATTAGCATCCACTCCTATGGTA	2340
GCACACTGTTGACAAATAGGACAAGGGATAGGGGTTGACTATCCCTTATCCAAAATGCTTG	2400
GGACTAGAAGAGTTTTGGATTTTAGAGTCTTTTCAGGCATAGGTATATTTGAGTATATAT	2460
AAAATGAGATATCTTGGGGATGGGGCCCCAAGTATAAACATGAAGTTCATTTATATTTTCAT	2520
AATACCGTATAGACACTGCTTGAAGTGTAGTTTATACAGTGTTTTAAATAACGTTGTAT	2580
GCGTGAAGAGACGTTTTTACAGCATGAACCTGTCTACTCATGCCAGCACTCAAAAACCTTG	2640
GGGTTTTTGGAGCAGTTTGGATCTTGGGTTTTCTGTGTTAAGAGATGGTTAGCTTATACCTAA	2700
AACCATAATGGCAAACAGGCTGCAGGACCAGCTGGATCCTCAGCCCTGAAGTGTGCCCT	2760
TCCAGCCAGGTCATACCCTGTGGAGGTGAGCGGGATCAGGTTTTGTGGTGCTAAGAGAGG	2820
AGTTGGAGGTAGATTTTGGAGGATCTGAGGGC	2852

---G---GTTG CAAGGCCCAA GAAGCCCA-- -TCCTGGGAA GGAAAATGCA	50
TTGGGGAACC CTGTG-CGGA TTCTTGTGGC TTTGGCCCTA TCTTTTCTAT	100
GTCCAAGCTG TGCCCATCCA AAAAGTCCAA GATGACACCA AAACCCTCAT	150
CAAGACAATT GTCACCAGGA TCAATGACAT TTCACACACG CAGTCAGTCT	200
CCTCCAAACA GAAAGTCACC GGTTTGGACT TCATTCTGCTG GCTCCACCCC	250
ATCCTGACCT TATCCAAGAT GGACCAGACA CTGGCAGTCT ACCAACAGAT	300
CCTCACCAGT ATGCCTTCCA GAAACGTGAT CCAAATATCC AACGACCTGG	350
AGAACCTCCG GGATCTTCTT CACGTGCTGG CTTTCTCTAA GAGCTGCCAC	400
TTGCCCTGGG CCAGTGGCCT GGAGACCTTG GACAGCCTGG GGGGTGTCCT	450
GGAAGCTTCA GGCTACTCCA CAGAGGTGGT GGCCCTGAGC AGGCTGCAGG	500
GGTCTCTGCA GGACATGCTG TGGCAGCTGG ACCTCAGCCC TGGGTGCTGA	550
GGCCTTGAAG GTCACCTCTC CTGCAAGGAC T-ACGTTAAG GGAAGGAACT	600
CTGGTTTCCA GGTATCTCCA GGATTGAAGA GCATTGCATG GACACCCCTT	650
ATCCAGGACT CTGTCAATTT CCCTGACTCC TCTAAGCCAC TCTTCCAAAG	700
G	701

FIG.2

1 MET HIS TRP GLY THR LEU CYS GLY PHE LEU TRP LEU TRP PRO TYR
16 LEU PHE TYR VAL GLN ALA VAL PRO ILE GLN LYS VAL GLN ASP ASP
31 THR LYS THR LEU ILE LYS THR ILE VAL THR ARG ILE ASN ASP ILE
46 SER HIS THR GLN SER VAL SER SER LYS GLN LYS VAL THR GLY LEU
61 ASP PHE ILE PRO GLY LEU HIS PRO ILE LEU THR LEU SER LYS MET
76 ASP GLN THR LEU ALA VAL TYR GLN GLN ILE LEU THR SER MET PRO
91 SER ARG ASN VAL ILE GLN ILE SER SER ASN ASP LEU GLU ASN LEU ARG
106 ASP LEU LEU HIS VAL LEU ALA PHE SER LYS SER CYS HIS LEU PRO
121 TRP ALA SER GLY LEU GLU THR LEU ASP SER LEU GLY GLY VAL LEU
136 GLU ALA SER GLY TYR SER THR GLU VAL VAL ALA LEU SER ARG LEU
151 GLN GLY SER LEU GLN ASP MET LEU TRP GLN LEU ASP LEU SER PRO
166 GLY CYS END

FIG. 3

MOUSE	MCWRPLCRFL	WLWSYLSYVQ	AVPIQKVODD	TKTLIKTI VT	RINDISHTQS	50
	* ** *	* *				
HUMAN	MHWGTLGGFL	WLWPYLFYVQ	AVPIQKVODD	TKTLIKTI VT	RINDISHTQS	
MOUSE	VSAKQRTGL	DFIPGLHPIL	SLSKMDQTLA	VYQQVL TSLP	SONVLQIAND	100
	*	-	-	-	*	
HUMAN	VSSKQKVTGL	DFIPGLHPIL	TLSKMDQTLA	VYQQIL TSMP	SRNVIOISND	
MOUSE	LENLRDLLHL	LAFSKSCSLP	QTSGLOK PES	LDGVLEASLY	STEVVALSRL	150
	-	*	** ***-	*	*	
HUMAN	LENLRDLLHV	LAFSKSCHLP	WASGLETLDS	LGGVLEASGY	STEVVALSRL	
MOUSE	OGSLODILQO	LDVSPEC				167
	- *	- *				
HUMAN	OGSLODMLWQ	LDLSPGC				

FIG.4

1	MET CYS TRP ARG PRO LEU CYS ARG PHE LEU TRP LEU TRP SER TYR
16	LEU SER TYR VAL GLN ALA VAL PRO ILE GLN LYS VAL GLN ASP ASP
31	THR LYS THR LEU ILE LYS THR ILE VAL THR ARG ILE ASN ASP ILE
46	SER HIS THR SER VAL SER ALA LYS GLN ARG VAL THR GLY LEU ASP
61	PHE ILE PRO GLY LEU HIS PRO ILE LEU SER LEU SER LYS MET ASP
76	GLN THR LEU ALA VAL TYR GLN GLN VAL LEU THR SER LEU PRO SER
91	GLN ASN VAL LEU GLN ILE ALA ASN ASP LEU GLU ASN LEU ARG ASP
106	LEU LEU HIS LEU LEU ALA PHE SER LYS SER CYS SER LEU PRO GLN
121	THR SER GLY LEU GLN LYS PRO GLU SER LEU ASP GLY VAL LEU GLU
136	ALA SER LEU TYR SER THR GLU VAL VAL ALA LEU SER ARG LEU GLN
151	GLY SER LEU GLN ASP ILE LEU GLN GLN LEU ASP VAL SER PRO GLU
166	CYS END

FIG.5

1 MET HIS TRP GLY THR LEU CYS GLY PHE LEU TRP LEU TRP PRO TYR
16 LEU PHE TYR VAL GLN ALA VAL PRO ILE GLN LYS VAL GLN ASP ASP
31 THR LYS THR LEU ILE LYS THR ILE VAL THR ARG ILE ASN ASP ILE
46 SER HIS THR SER VAL SER SER LYS GLN LYS VAL THR GLY LEU ASP
61 PHE ILE PRO GLY LEU HIS PRO ILE LEU THR LEU SER LYS MET ASP
76 GLN THR LEU ALA VAL TYR GLN GLN ILE LEU THR SER MET PRO SER
91 ARG ASN VAL ILE GLN ILE SER ASN ASP LEU GLU ASN LEU ARG ASP
106 LEU LEU HIS VAL LEU ALA PHE SER LYS SER CYS HIS LEU PRO TRP
121 ALA SER GLY LEU GLU THR LEU ASP SER LEU GLY GLY VAL LEU GLU
136 ALA SER GLY TYR SER THR GLU VAL VAL ALA LEU SER ARG LEU GLN
151 GLY SER LEU GLN ASP MET LEU TRP GLN LEU ASP LEU SER PRO GLY
166 CYS END

FIG.6

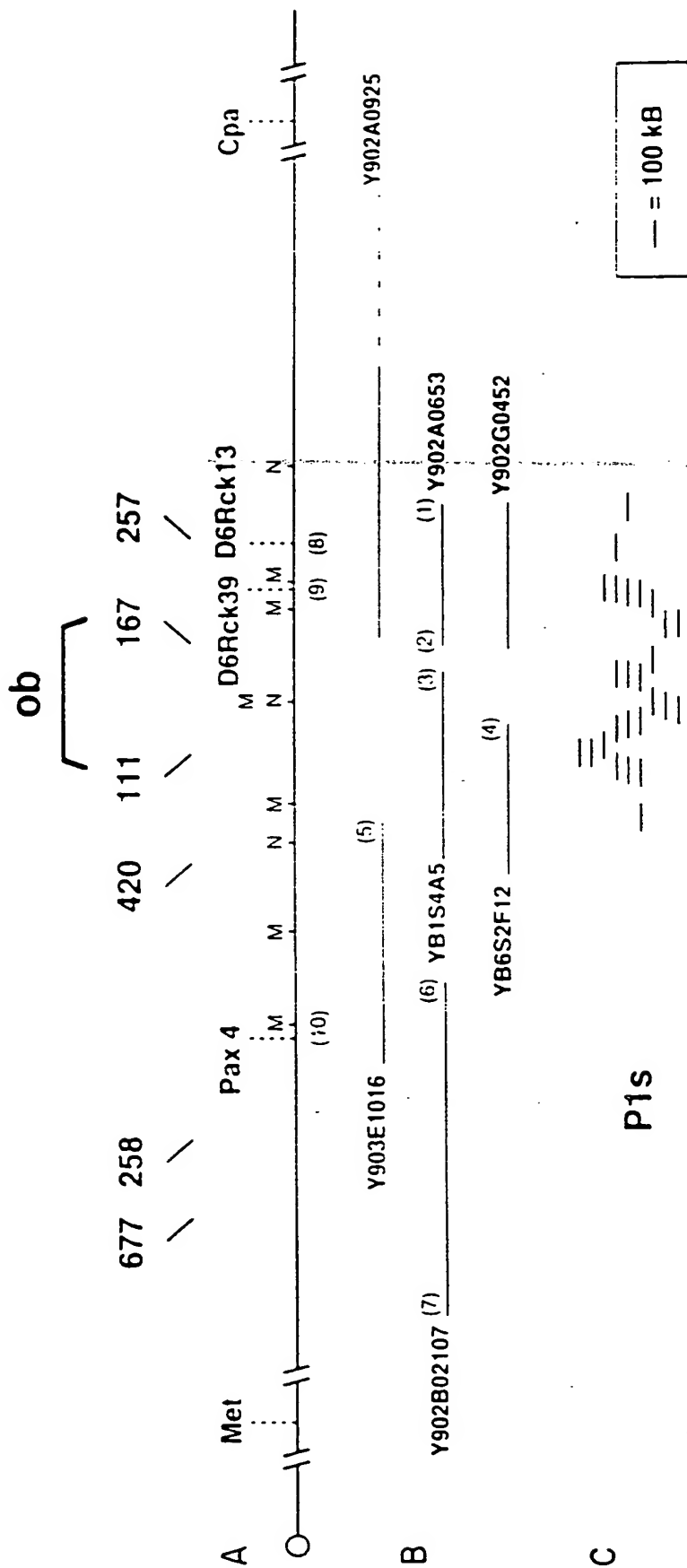


FIG.7

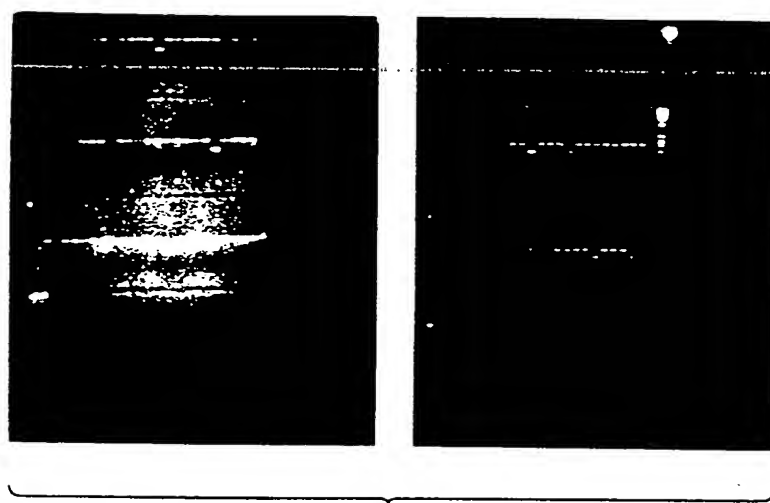


FIG.8



FIG.9

1	+10	+20	+30	+40
	GTGCAAGAAG	AAGAAGATCC	<u>CAGGGCAGGA</u>	AAATGTGCTG GAGACCCCTG
	-----	-----	-----	-----
	CAGGTCTTC	TTCTTCTAGG	GTCCCGTCCT	TTTACACGAC CTCTGGGGAC
	-----	-----	-----	-----
51	+10	+20	+30	+40
	TGTCGGGTCC	NGTGGNTTTG	GTCCCTATCTG	TCTTATGTNC AAGCAGTGCC
	-----	?	-----	?
	ACAGCCCAGG	NCACCNAAAC	CAGGATAGAC	AGAATACANG TTCGTCACGG
	-----	-----	-----	-----
101	+10	+20	+30	+40
	TATCCAGAAA	GTCCAGGATG	ACACCAAAG	CCTCATCAAG ACCATTGTCA
	-----	-----	-----	-----
	<u>ATAGGTCCTT</u>	<u>CAGGTCCTAC</u>	TGTGGTTTC	GGAGTAGTTC TGGTAACAGT
	-----	-----	-----	-----
151	+10	+20	+30	+40
	NCAGGATCAC	TGANATTTC	CACACG	
	?	-----	-----	-----
	NGTCCTAGTG	ACTNTAAAGT	GTGTGC	

FIG.10

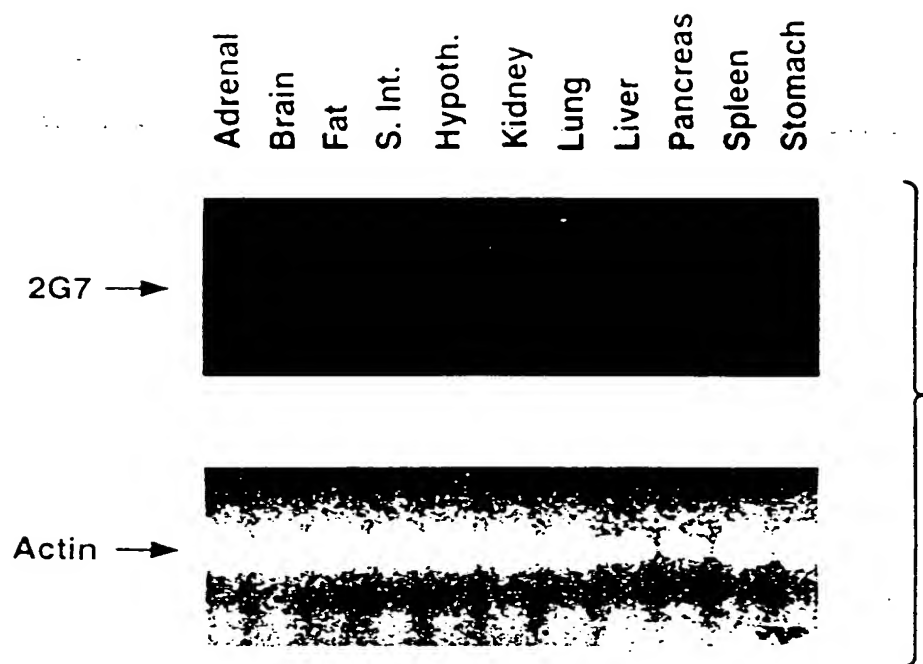


FIG.11A

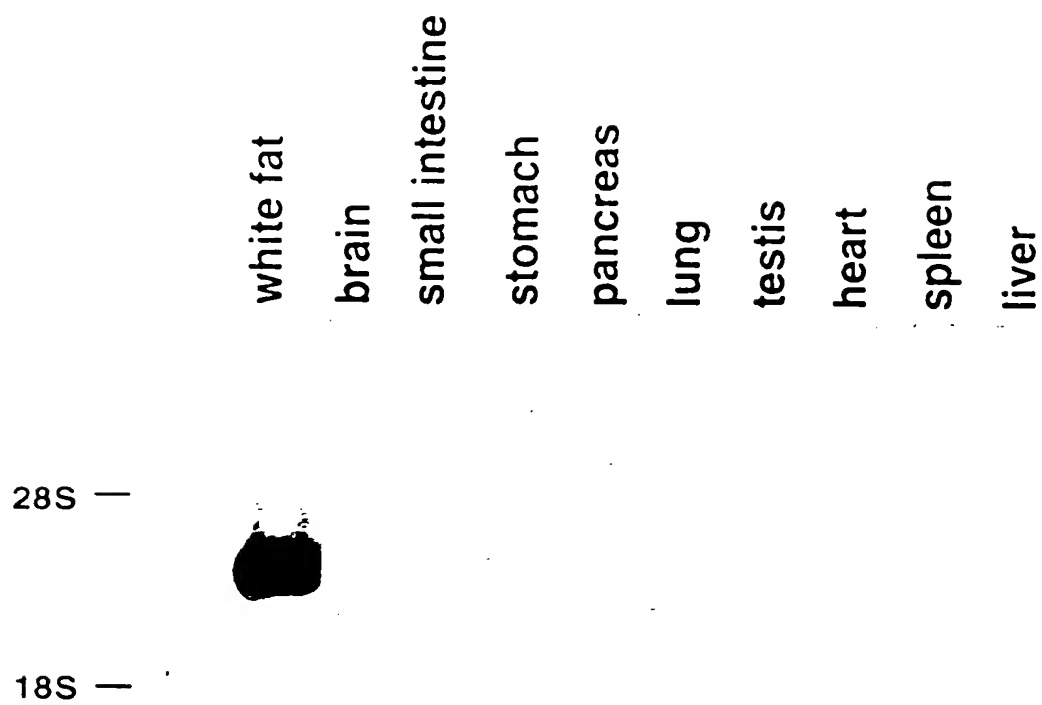


FIG.11B



FIG.12A

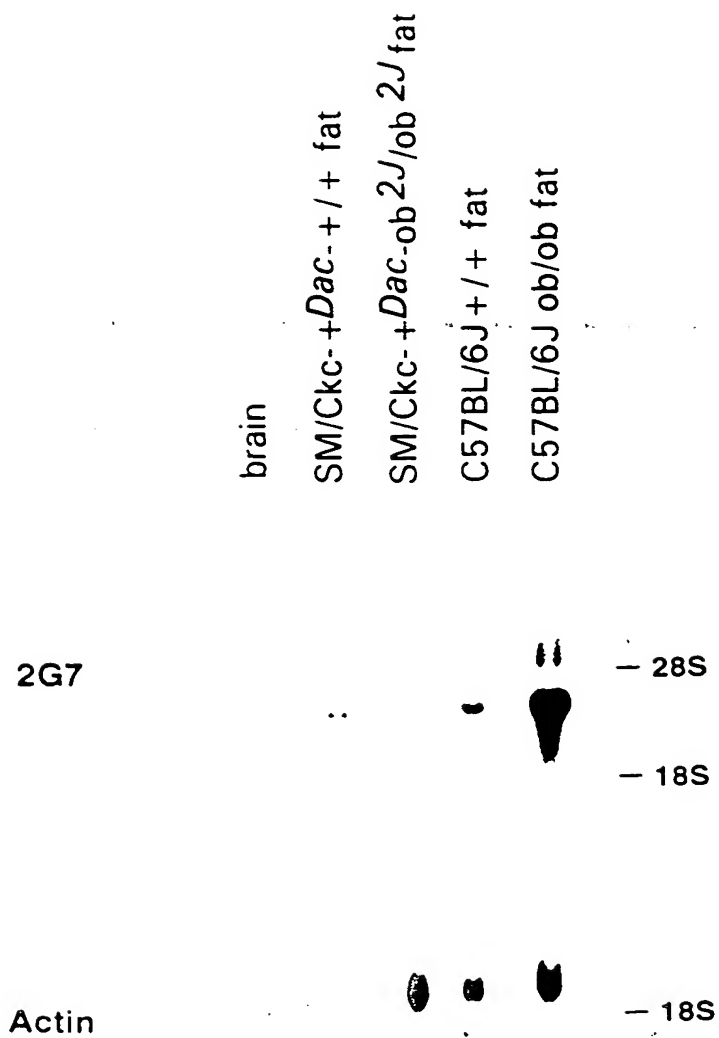


FIG. 12B

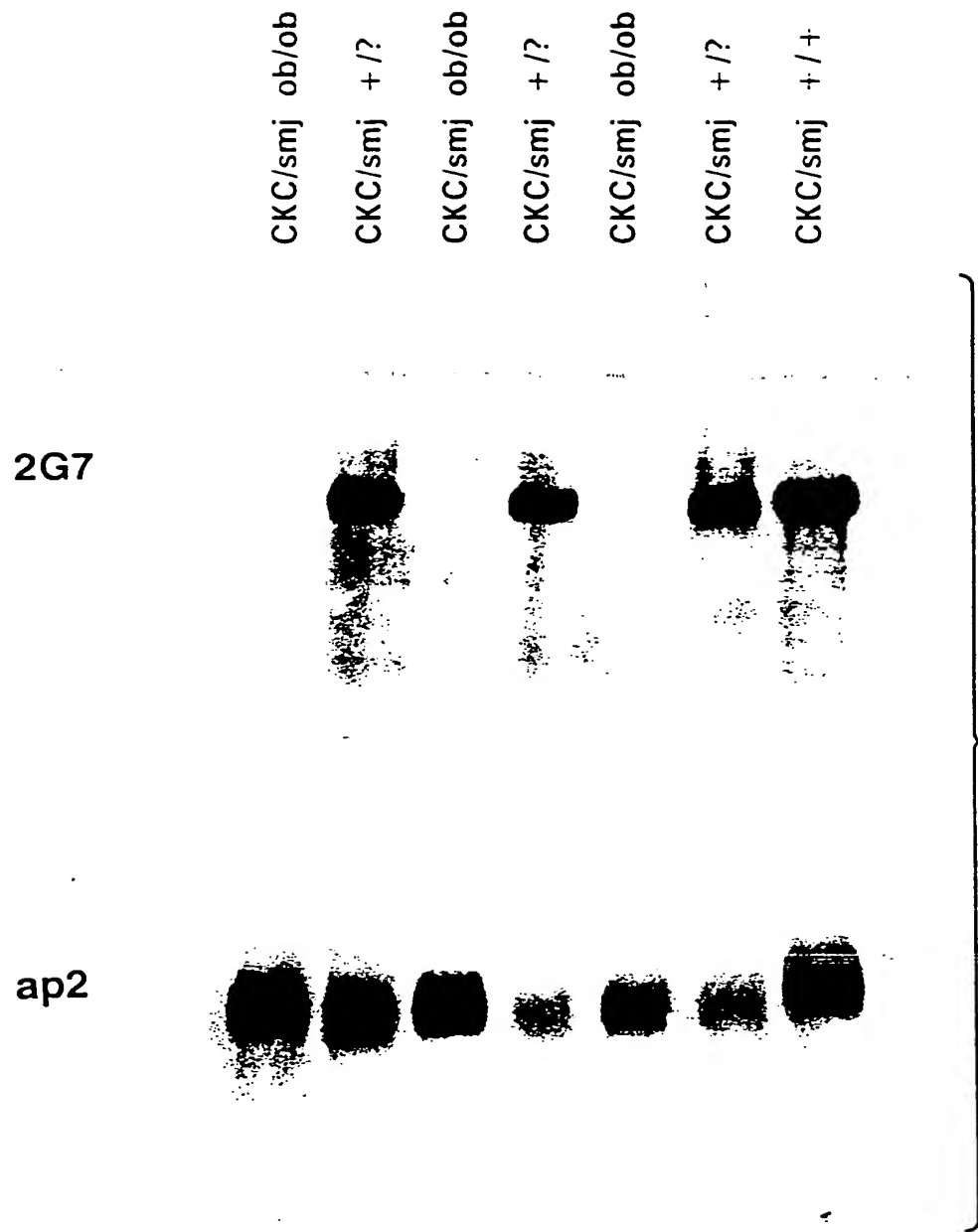
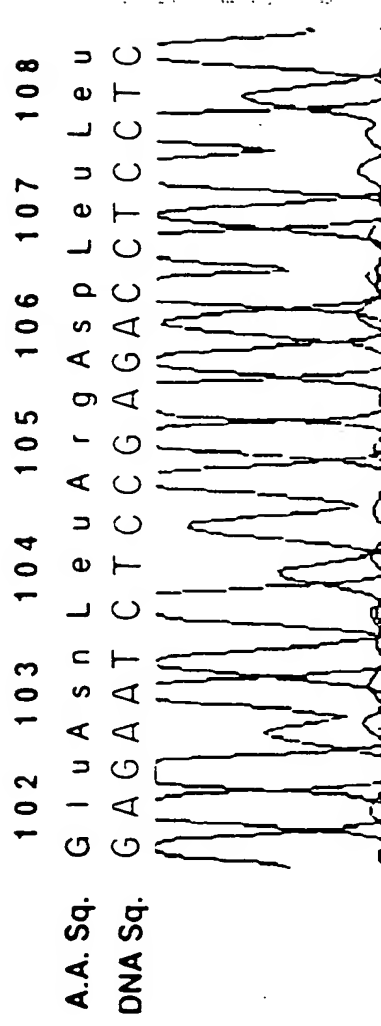
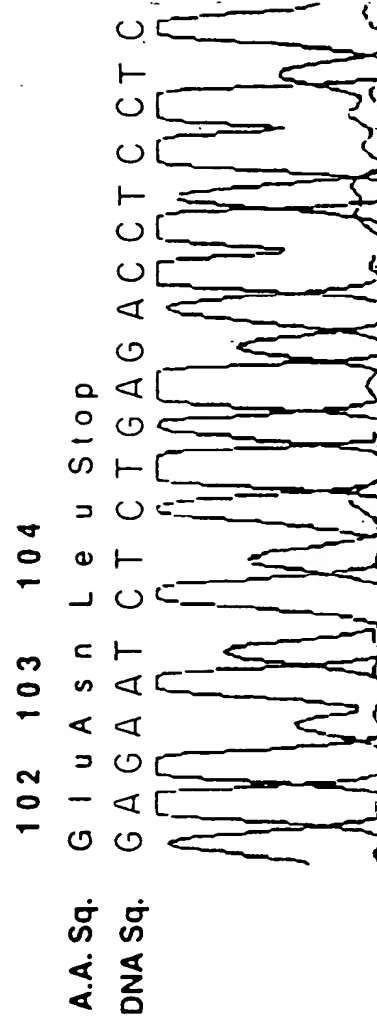


FIG.13



C57BL/6J



C57BL/6J ob/ob

FIG.14

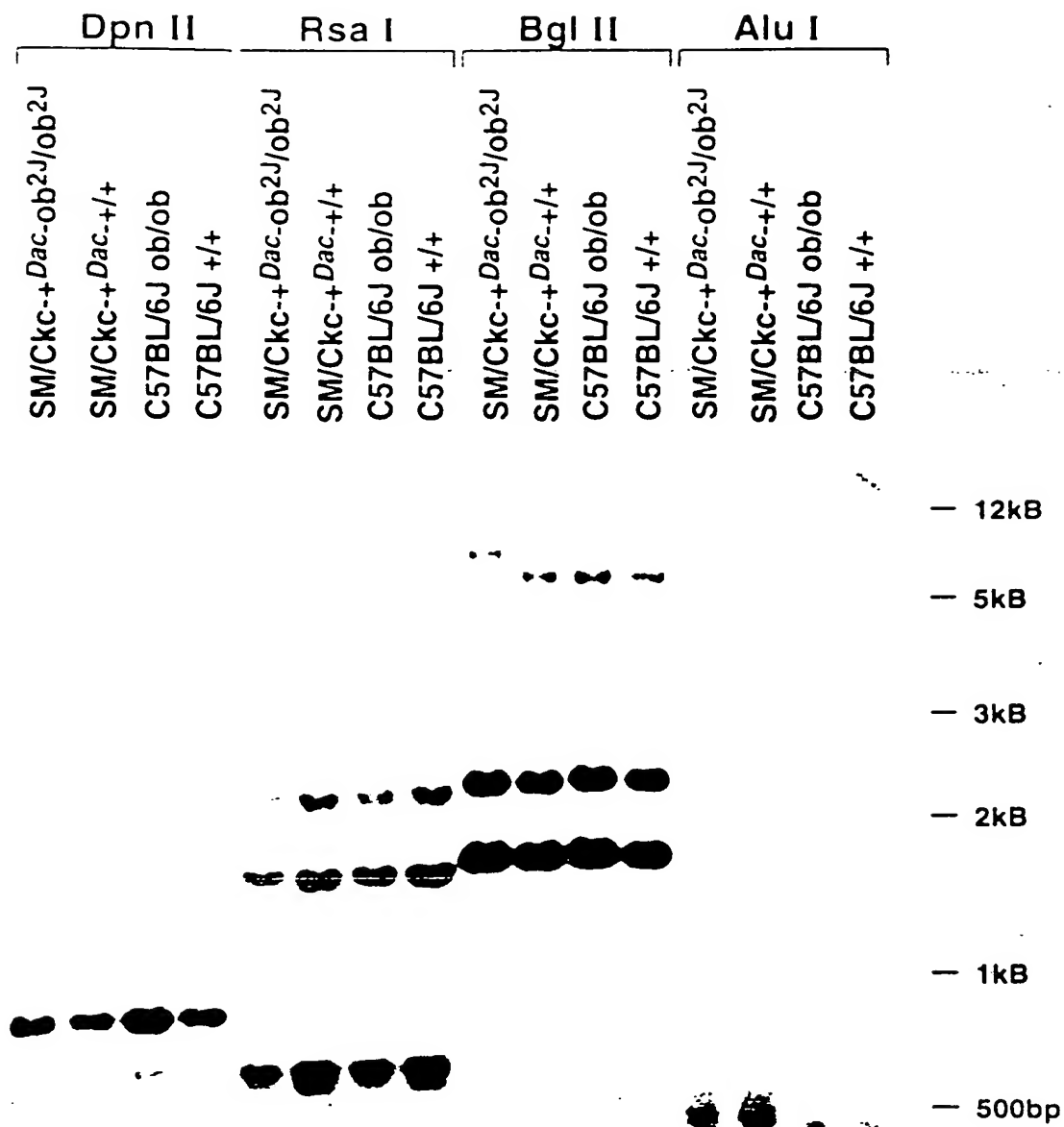


FIG.15A

BglII Digests

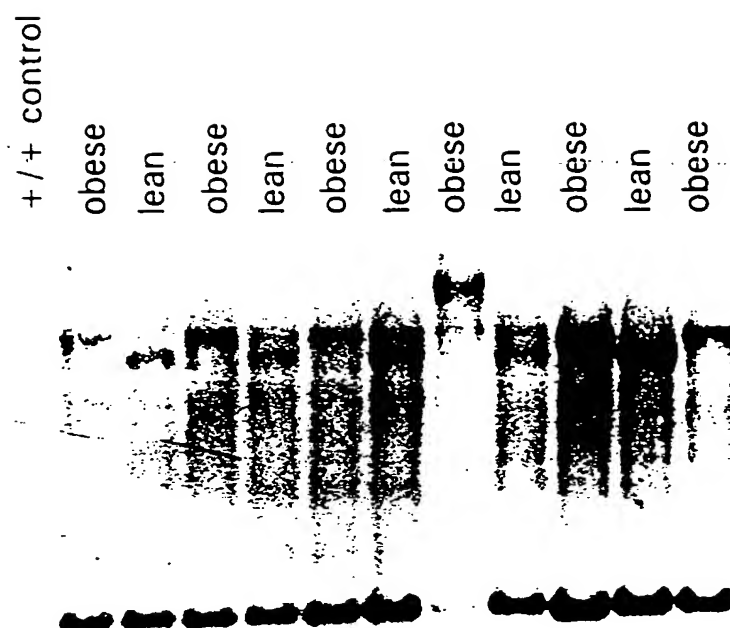


FIG.15B

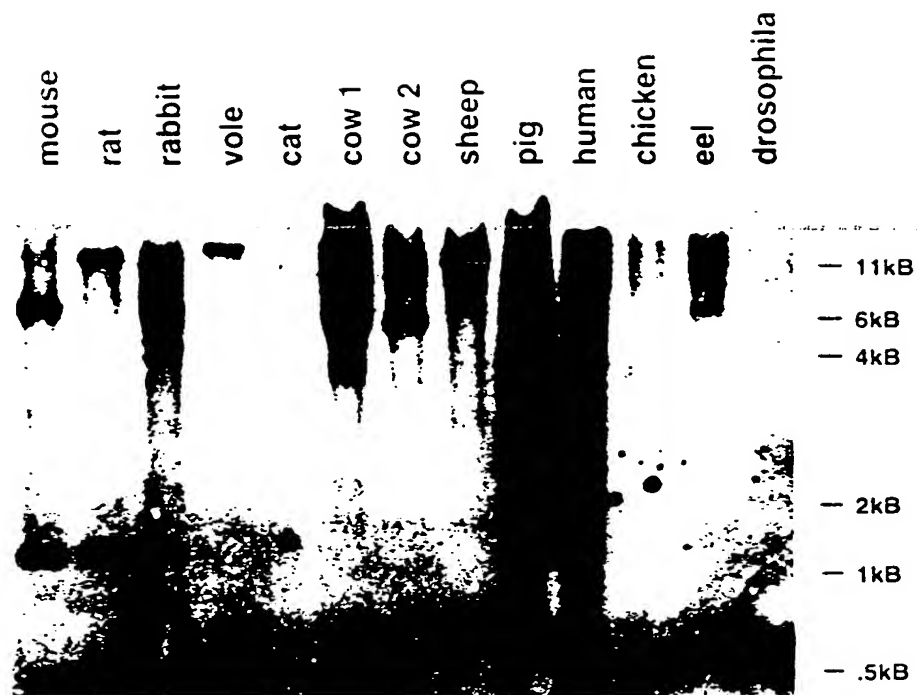


FIG.16

T7 PROMOTER PRIMER 69348-1

----->

T7 PROMOTER

BGLII

XBAI

LAC OPERATOR

----->

AGATCTCGATCCCGGAAATTAACGACTCACTATAGGGAATTGTGAGCGGATAACAATTCCTCTACA

RBS

NcoI

HIS-TAG

AATAATTTTGTAACTTTAAGAGGAGATATACCATGGGCAGCAGCCATCATCATCATCACAGCAGCGGC
METGLYSERSEHHISHISHISHISERSERGLY

NDEI

XHOI

BAMHI

CTGGTCCGCGGCAGCCATATGCTCGAGGATCCCGCTGCTAACAAAGCCGAAAGGAGCTGAGTTGGCT
LEUVALPROARGGLYSERHISMETLEUGLUASPPROALAAASNLYSALAARGLYSGLUALAGLULEUALA

THROMBIN

BPUI1021

T7 TERMINATOR

GCTGCCACCGCTGAGCAATAACTAGCATAACCCCTTGGGGCCTCTAAACGGGCTTGAGGGGTTTTTG
ALAAALATHRALAGLUGLNE

<-----

T7 TERMINATOR PRIMER #69337-1

FIG.17



FIG.18A

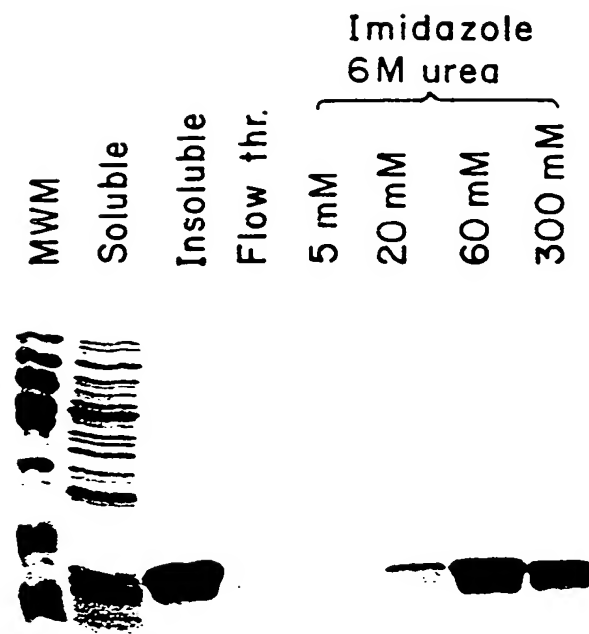


FIG.18B

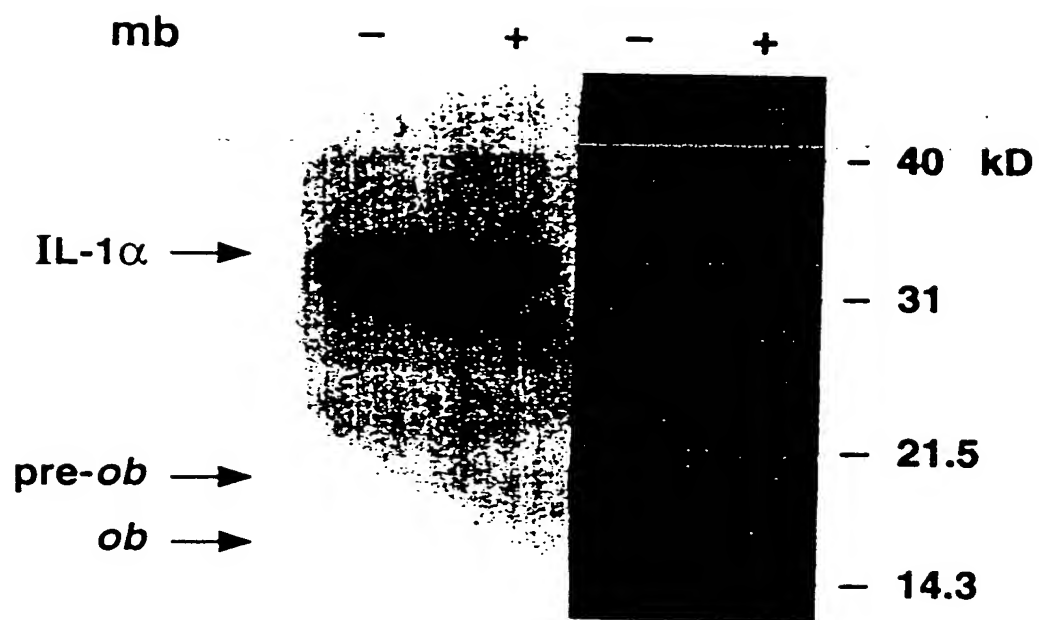


FIG.19A

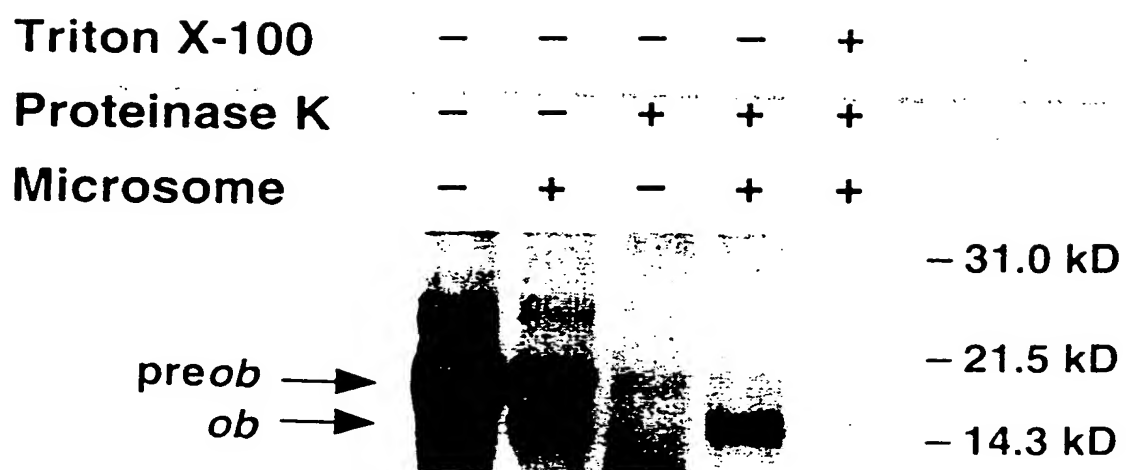


FIG.19B

10	20	30	40	50
<u>GGTTGCAAGG CCCAAGAAGC CCATCCTGGG AAGGAAATG CATTGGGGAA</u>				
HOB 1G F →				
START				
60	70	80	90	100
<u>CCCTGTGCGG ATTCTTGTGG CTTGGGCCCT ATCTTTTCTA TGTCCAAGCT</u>				
110	120	130	140	150
<u>GTGCCCCATCC AAAAGTCCA AGATGACACC AAAACCCTCA TCAAGACAAT</u>				
5' OF 1ST INTRON				
160	170	180	190	200
<u>TGTCACCAGG ATCAATGACA TTTCACACAC GGTAAGGAGA GTATGCGGGG</u>				
210	220	230	240	250
<u>ACAAAGTAGA ACTGCAGCCA GCCCAGCACT GGCTCCTAGT GGCACTGGAC</u>				
← HOB 1G R				

FIG.20A -1

260		270		280		290		300	
<u>CCAGATAGTC CAAGAAACAT TTATTGAACG CCTCCTGAAT GCCAGGCACC</u>									
310		320		330		340		350	
<u>TACTGGAAGC TGAGAAGGAT TTGGATAGC ACAGGGCTCC ACTCTTTCG</u>									
360		370		380		390		400	
<u>GTTGTTTCTT NIGGCCCCCT CTGCCCTGCTG AGATNCCAGG GGTTAGNGGT</u>									
410		420		430		440		450	
<u>TCTTAATTCC TAAA-----</u>									
GAP OF SEQUENCE (~1.4 KB)									
460		470		480		490		500	
<u>GGTTCITTCA GGAAGAGGCC ATGTAAGAGA AAGGAATTGA CCTAGGGAAA</u>									

FIG.20A - 2

510	520	530	540	550
<u>ATTGGCCTGG GAAGTGGAGG GAACGGATGG TGTGGGAAA GCAGGAATCT</u>				
560	570	580	590	600
<u>CGGAGACCAG CTTAGAGGCT TGGCAGTCAC CTGGGTGCAG GANACAAGGG</u>				
610	620	630	640	650
<u>CCTGAGCCAA AGTGGTGAGG GAGGGTGGAA GGAGACAGCC CAGAGAATGA</u>				
660	670	680	690	700
<u>CCCTCCATGC CCACGGGGAA GGACAGAGGC TCTGAGAGCG ATTCTCCCA</u>				
		3' OF 1ST INTRON ←		
710	720	730	740	750
<u>CATGCTGAGC ACTTGTTCTC CCCTCTTCCTC CTNCATAGCA GTCAGTCTCC</u>				
HOB 2G F →				

FIG.20A -3

760	770	780	790	800
<u>TCCAAACAGA AAGTCACCGG TTGGACITC ATTCTGGGC TCCACCCCAT</u>				
810	820	830	840	850
<u>CCTGACCTTA TCCAAGATGG ACCAGACACT GGCAGTCTAC CAACAGATCC</u>				
860	870	880	890	900
<u>TCACCAGTAT GCCTTCCAGA AACGTGATCC AAATATCCAA CGACCTGGAG</u>				
910	920	930	940	950
<u>AACCTCCGGG ATCTTCTTCA CGTGTGGCC TTCTCTAAGA GCTGCCACTT</u>				
960	970	980	990	1000
<u>GCCCTGGGCC AGTGGCCTGG AGACCTTGA CAGCCTGGG GGTGTCCTGG</u>				

FIG.20A -4

1010	1020	1030	1040	1050
<u>AAGCTTCAGG CTACTCCACA GAGGTGGTGG CCCTGAGCAG GCTGCAGGGG</u>				
1060	1070	1080	1090	1100
<u>TCTCTGCAGG ACATGCTGTG GCAGCTGGAC CTCAGCCCTG GGTGCTGAGG</u>				
STOP				
1110	1120	1130	1140	1150
<u>CCTTGAAGGT CACTCTTCCT GCAAGGACTA CGTTAAGGA AGGAACTCTG</u>				
1160	1170	1180	1190	1200
<u>GCTTCCAGGT ATCTCCAGGA TTGAAGAGCA TTGCATGGAC ACCCCTTATC</u>				
HOB 2G R				
1210	1220	1230	1240	1250
<u>CAGGACTCTG TCAATTTCCTC TGACTCCTCT AAGCCACTCT TCCAAAGG</u>				

FIG.20A -5

MOUSE OB STRUCTURE

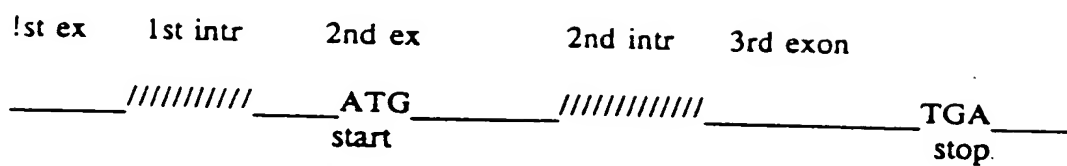


FIG.20B

HUMAN OB STRUCTURE

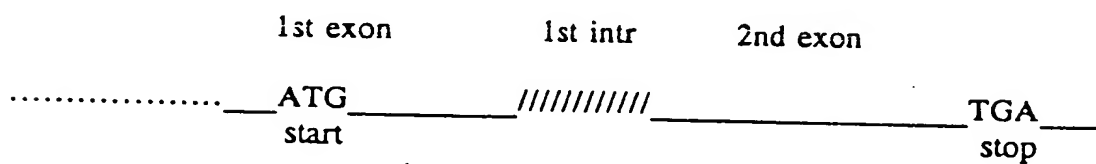


FIG.20C

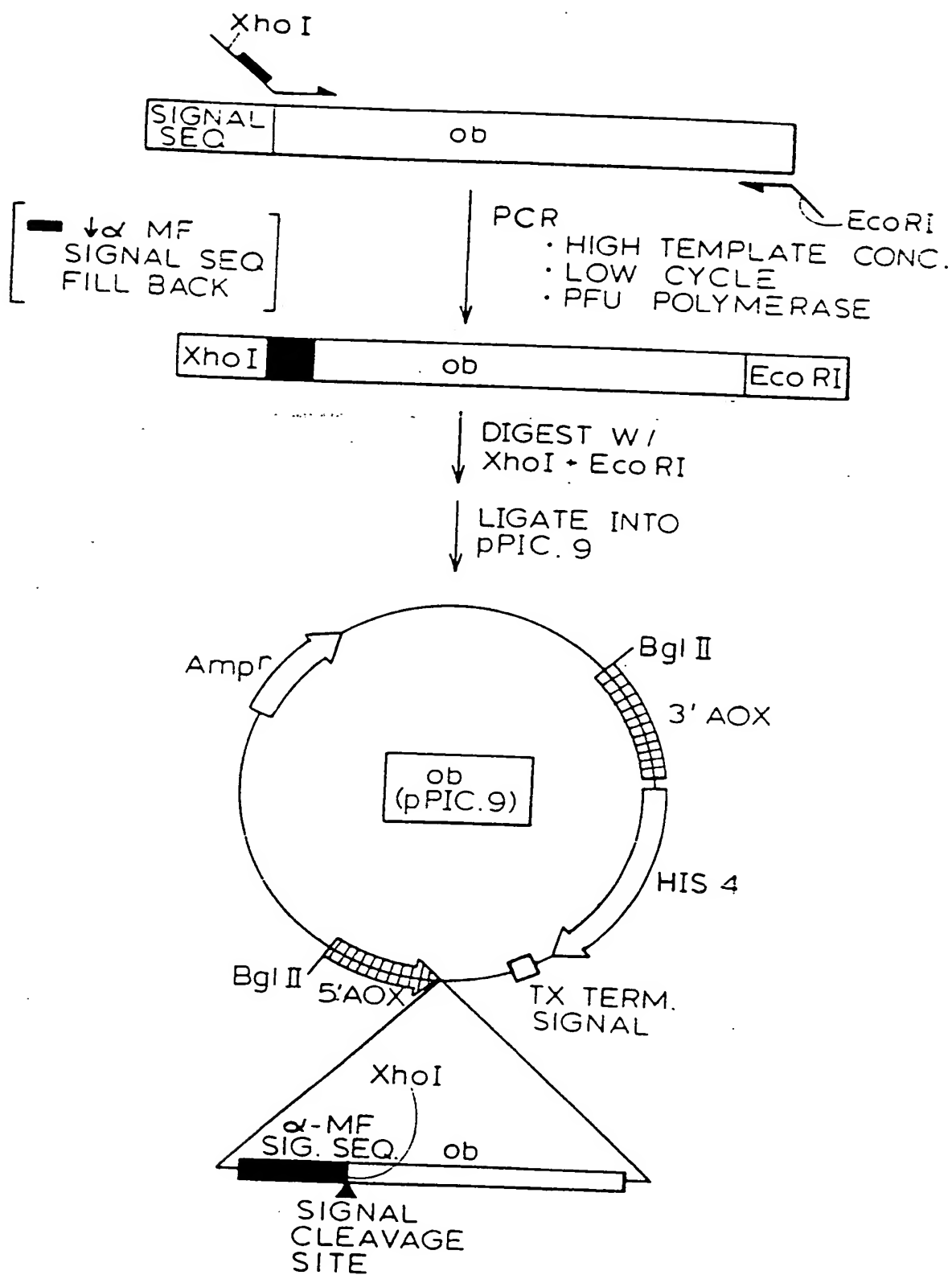


FIG.21A

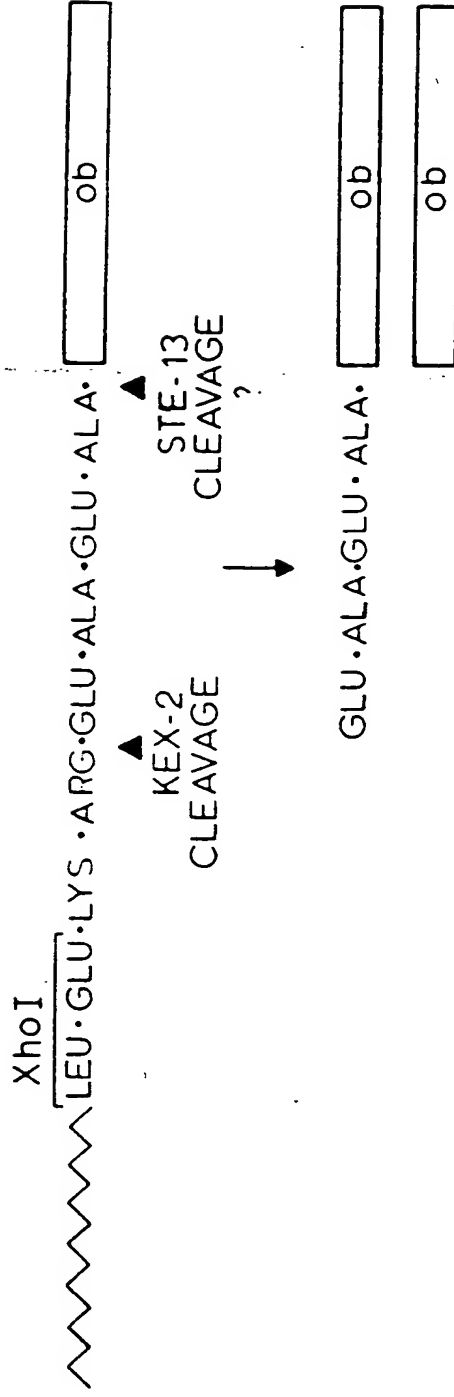


FIG.21B

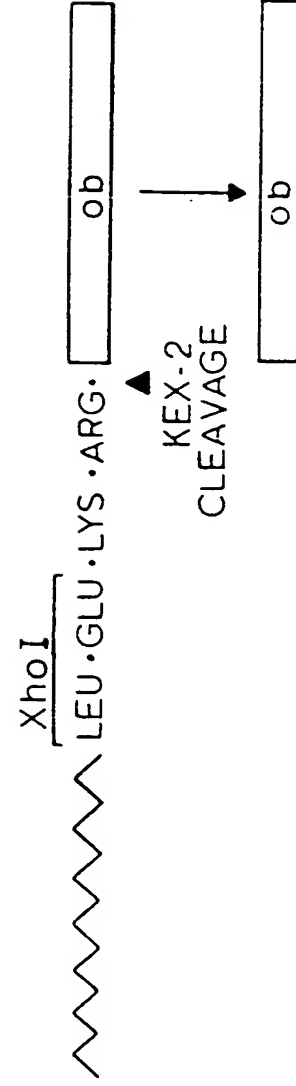


FIG.21C

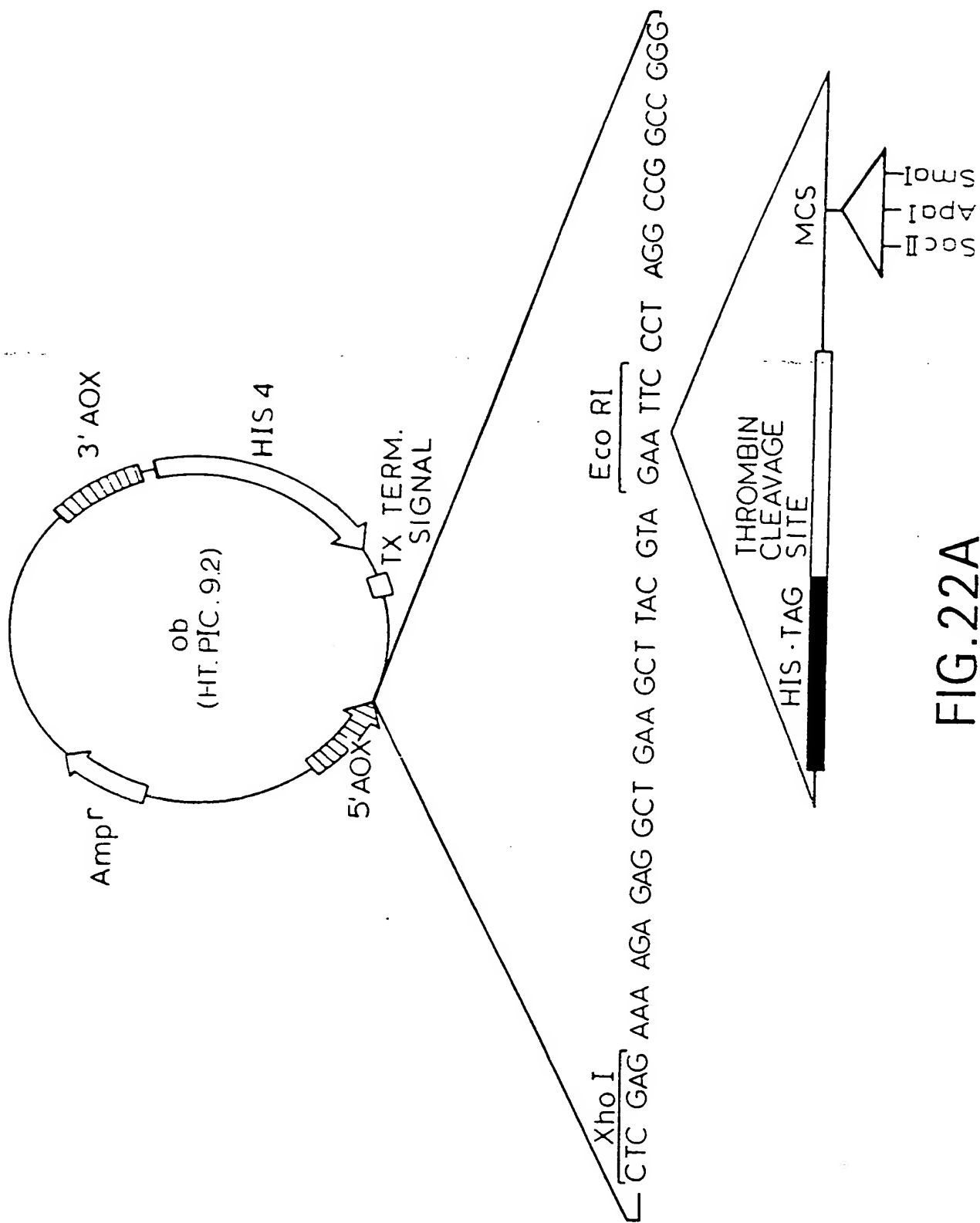


FIG. 22A

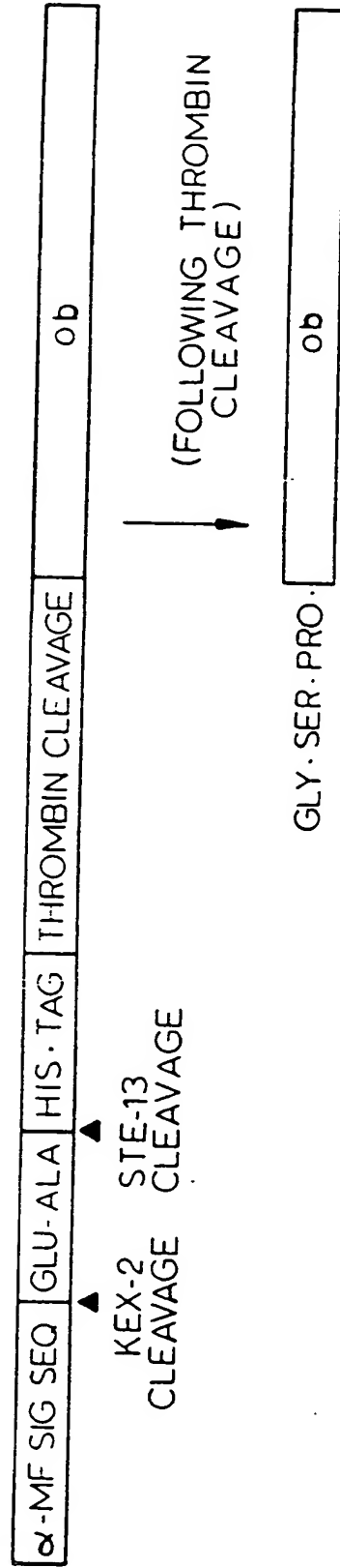


FIG. 22B

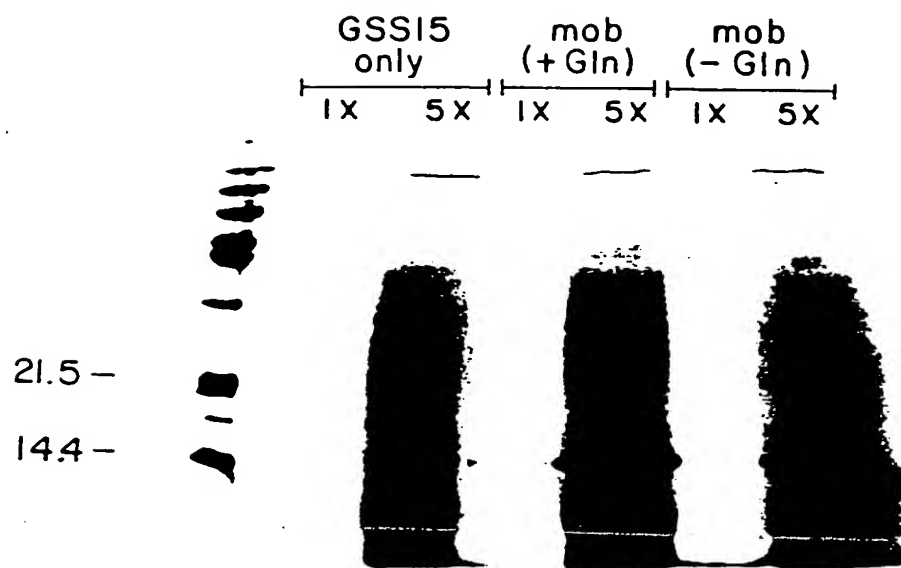


FIG.23A

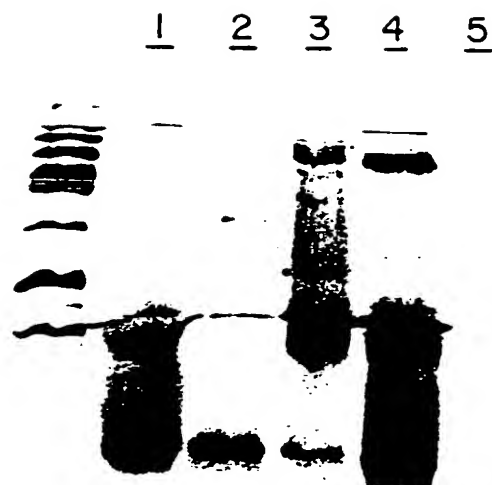


FIG.23B

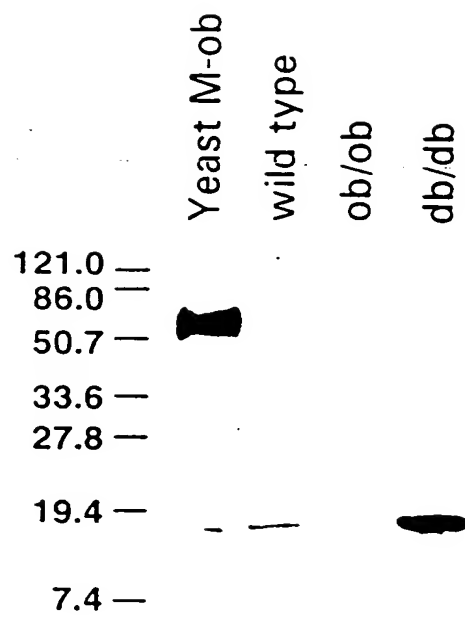


FIG.24A

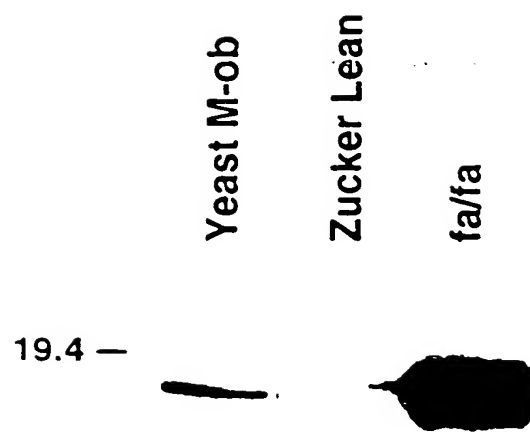


FIG.24B

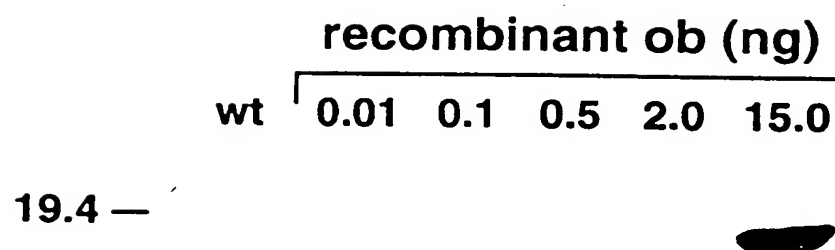


FIG.24C

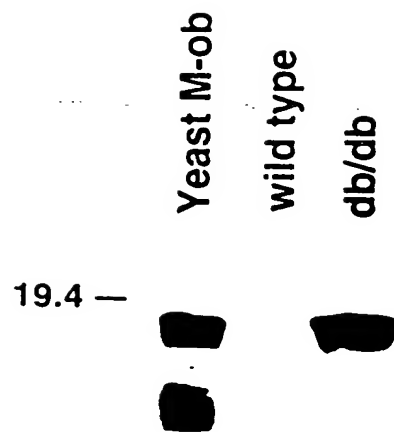


FIG.24D

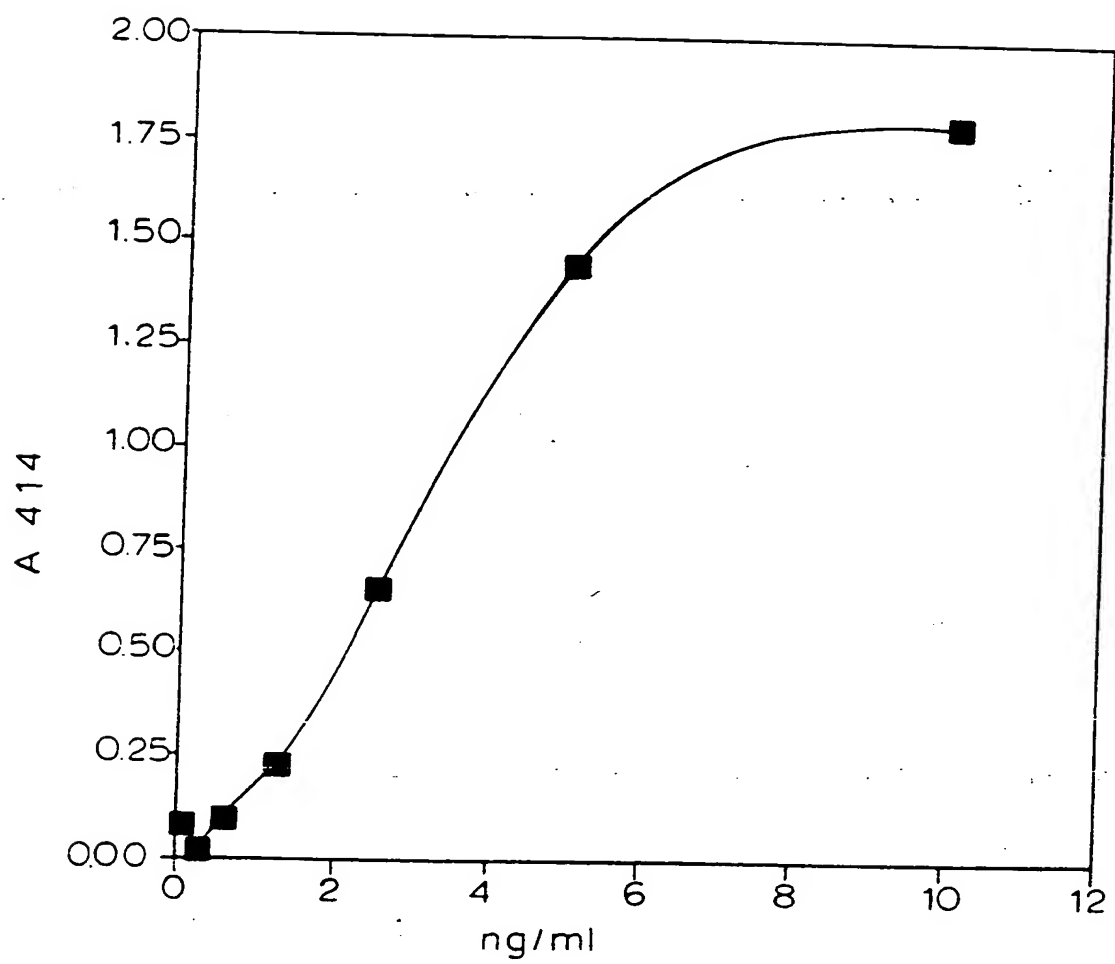


FIG.25B

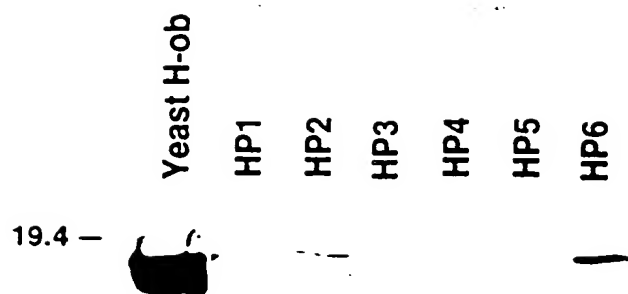


FIG.25A

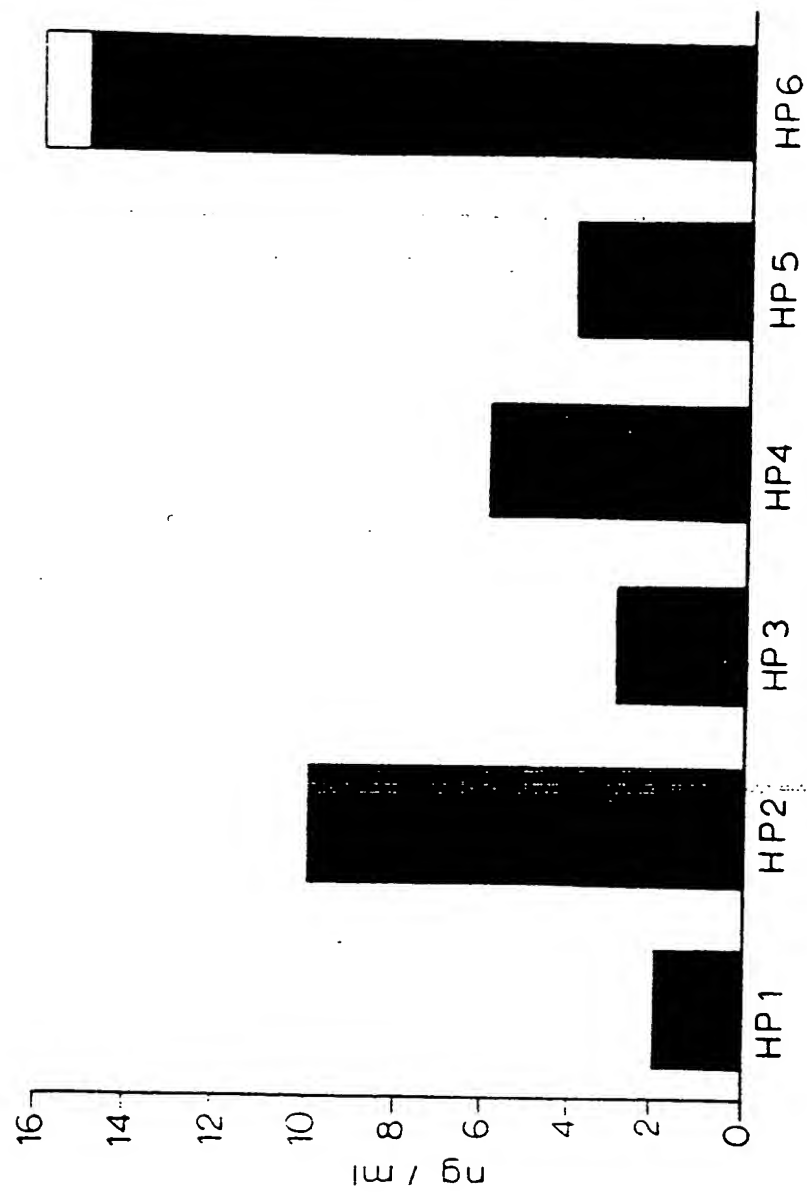


FIG.25C

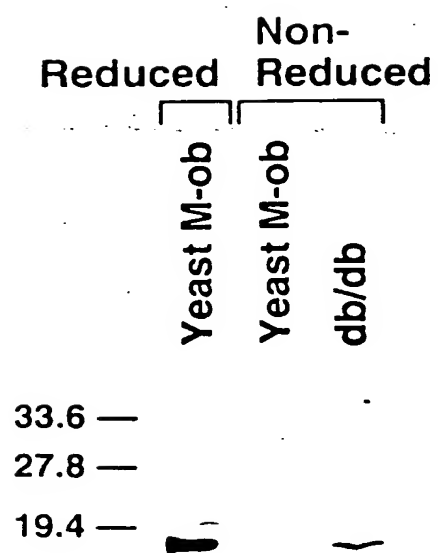
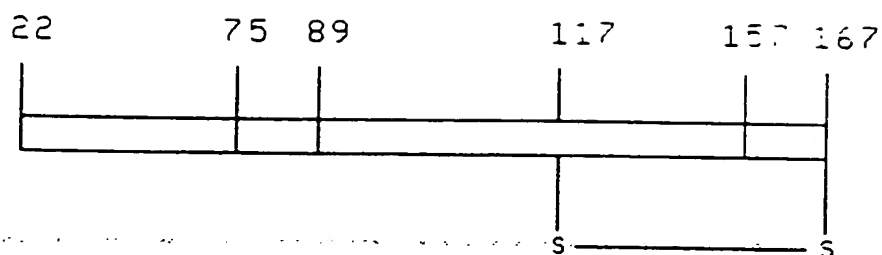


FIG.26A

Human ob



<u>Peptide</u>	<u>Mass(Da)</u>	
	Expected	Observed
22-167	16,024	16,024 \pm 3
22-75	5936.9	5936.6 \pm 1
76-89	1562.7	N.D.
90-167	8434.5	8435.6 \pm 1
158-167	1131.9	N.D.

FIG.26 B

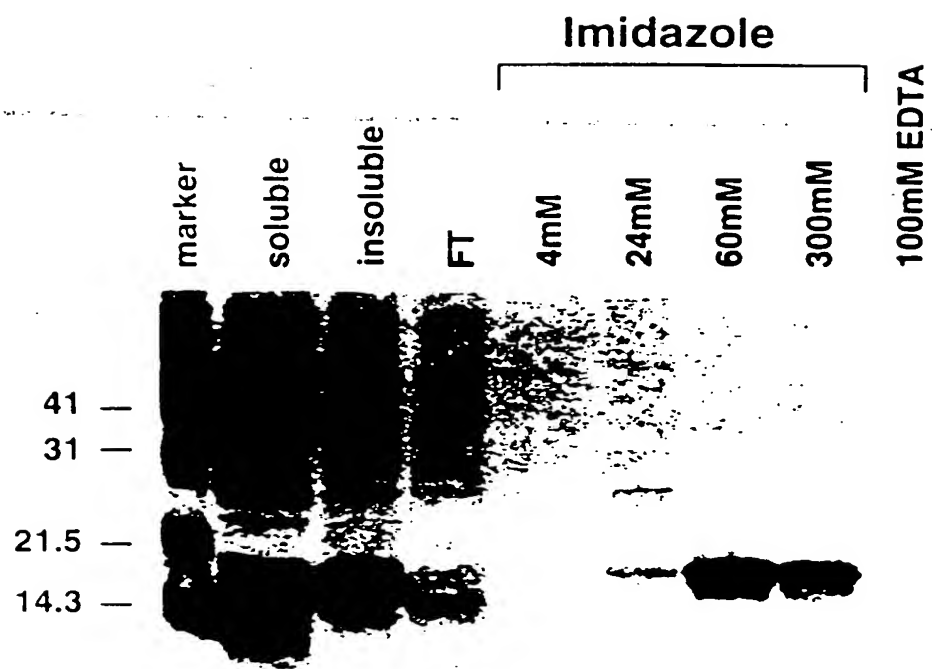


FIG.27

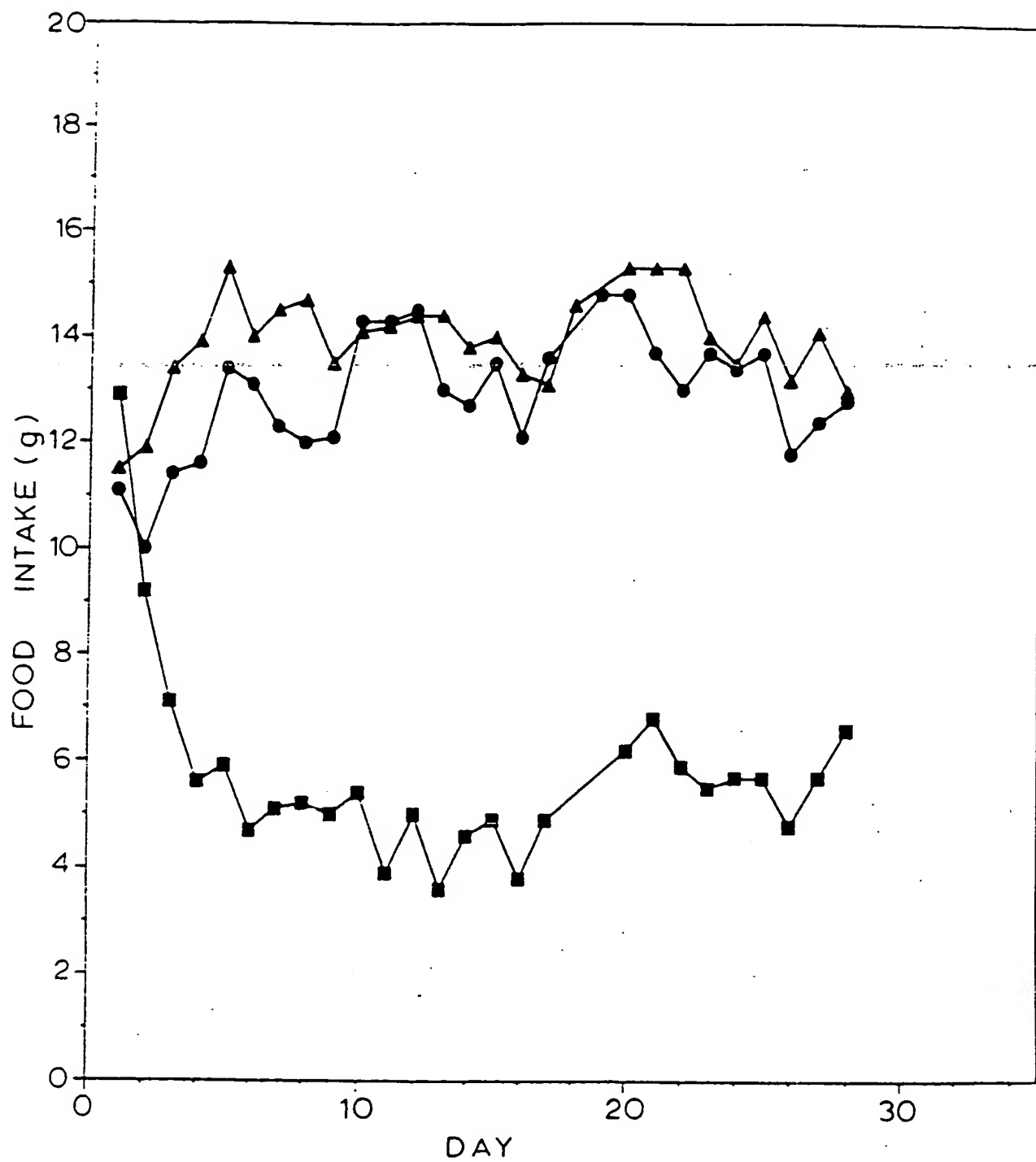


FIG.28A

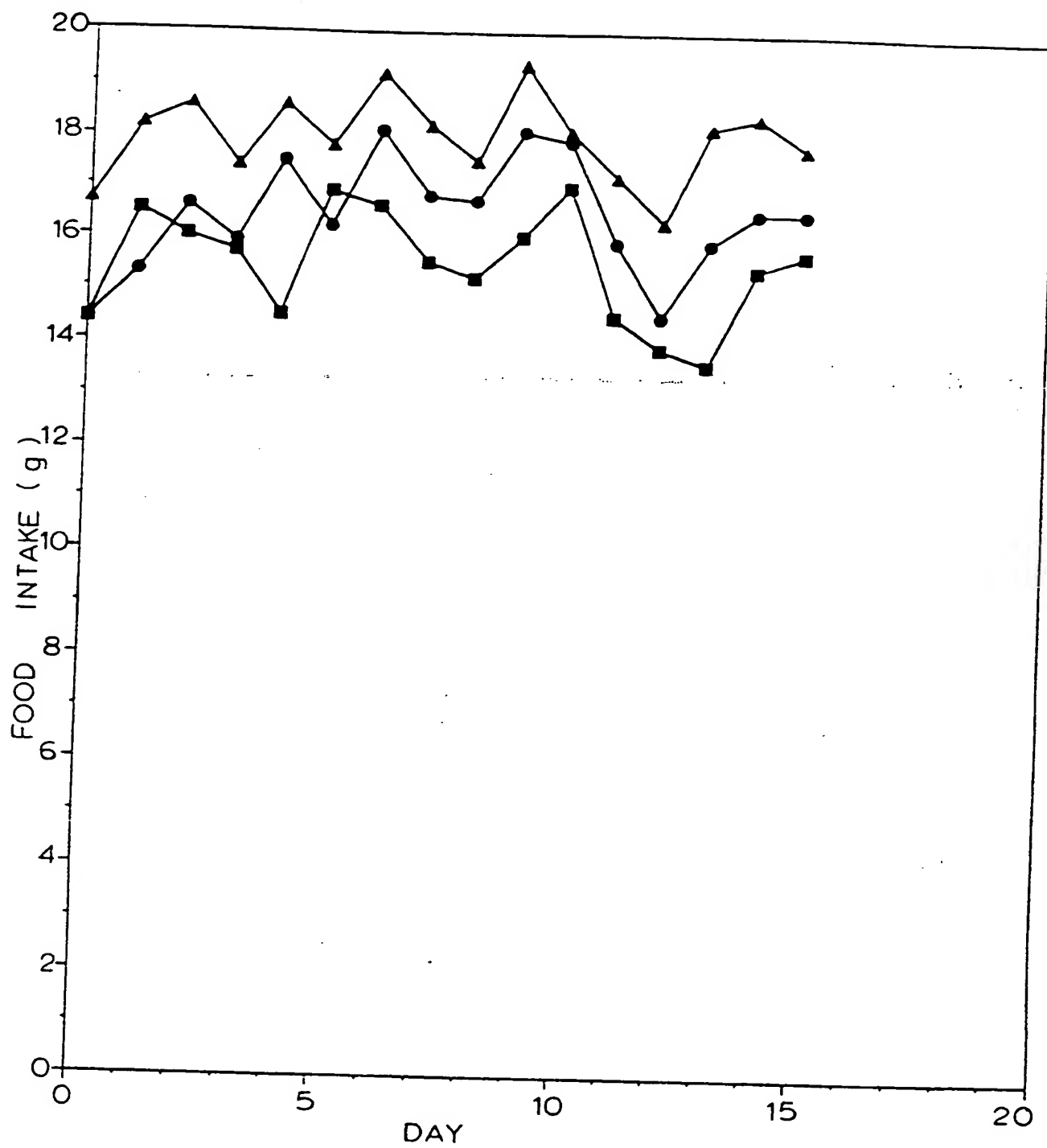


FIG.28B

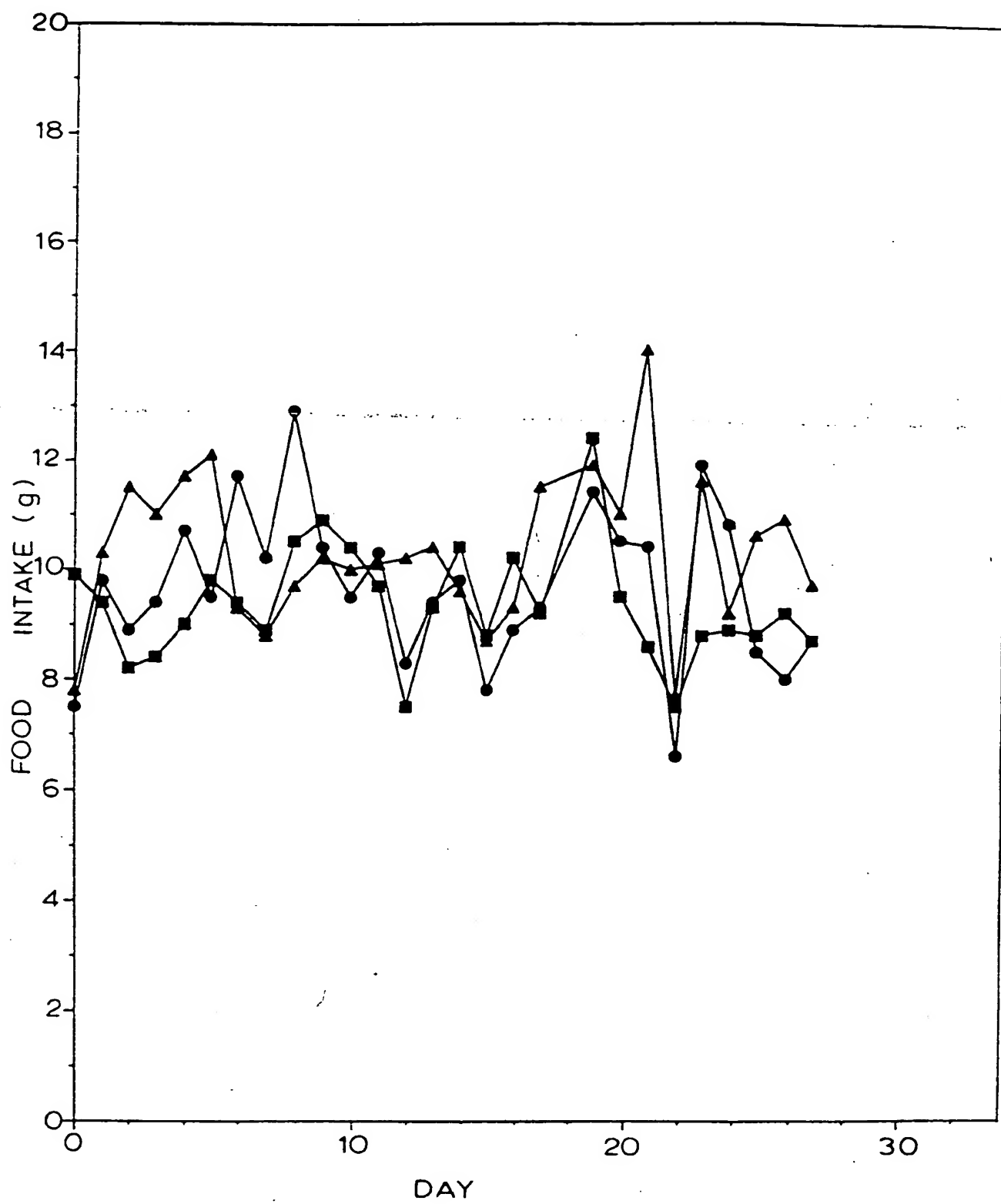


FIG.28C

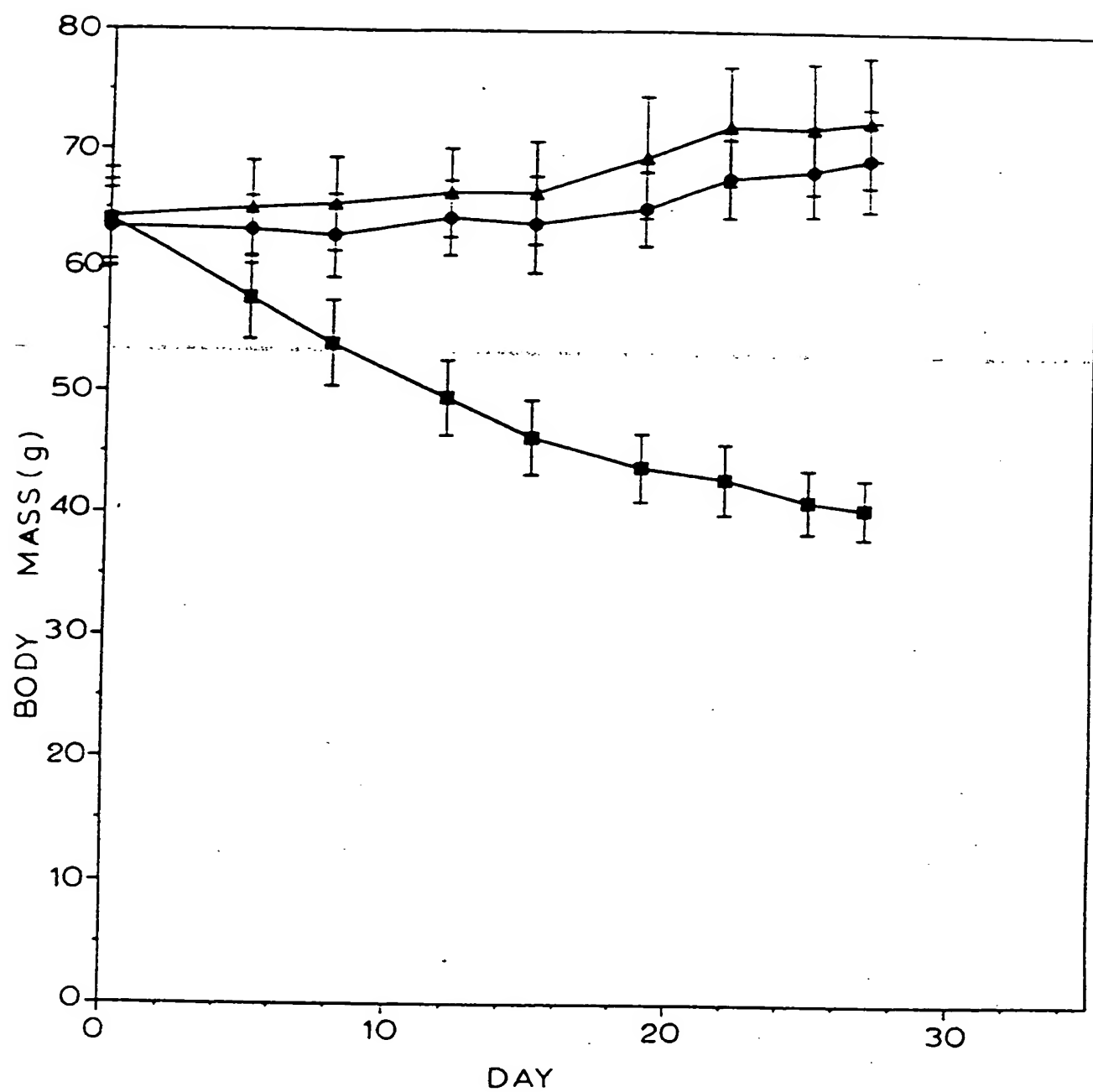


FIG.28D

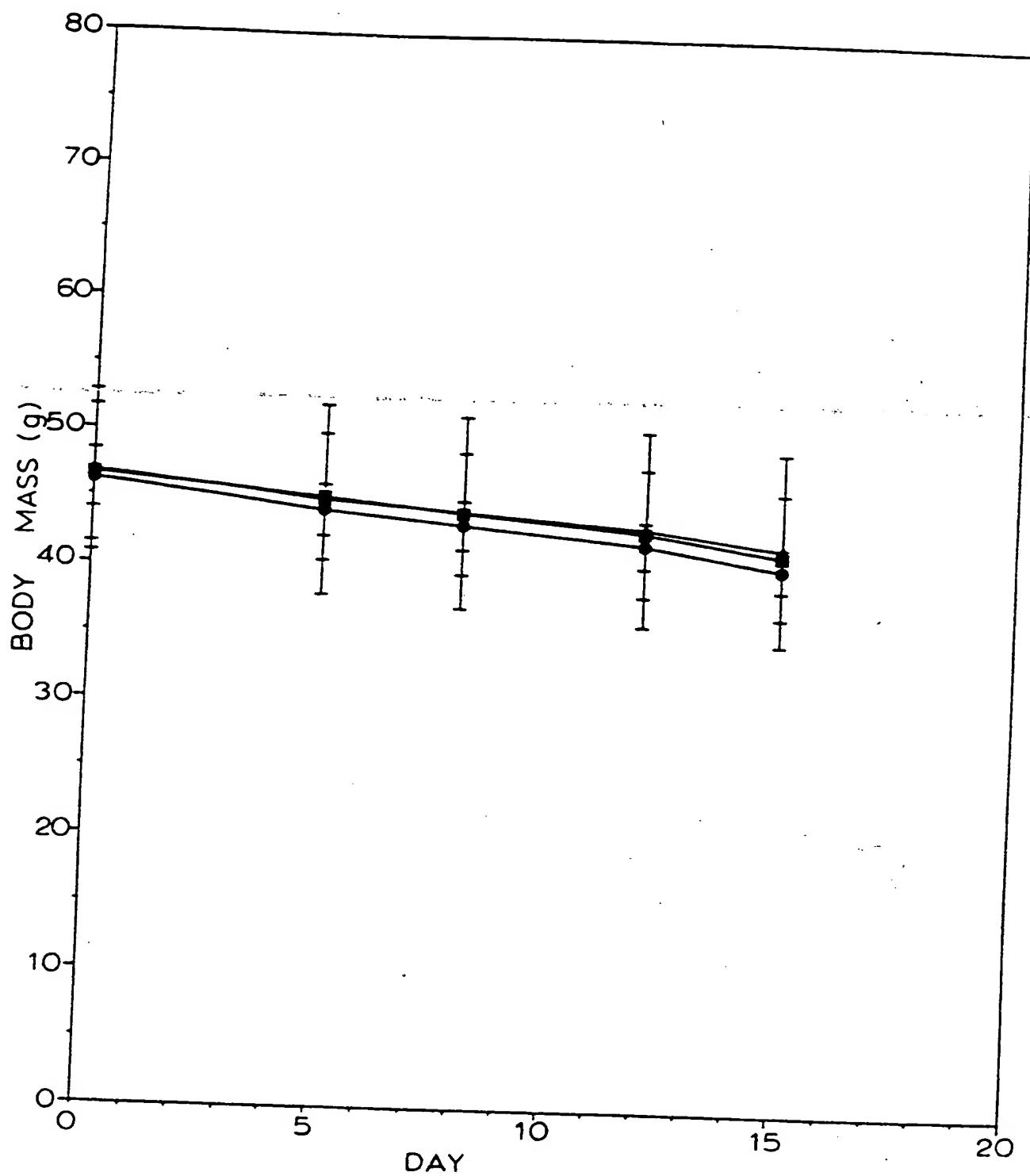


FIG.28E

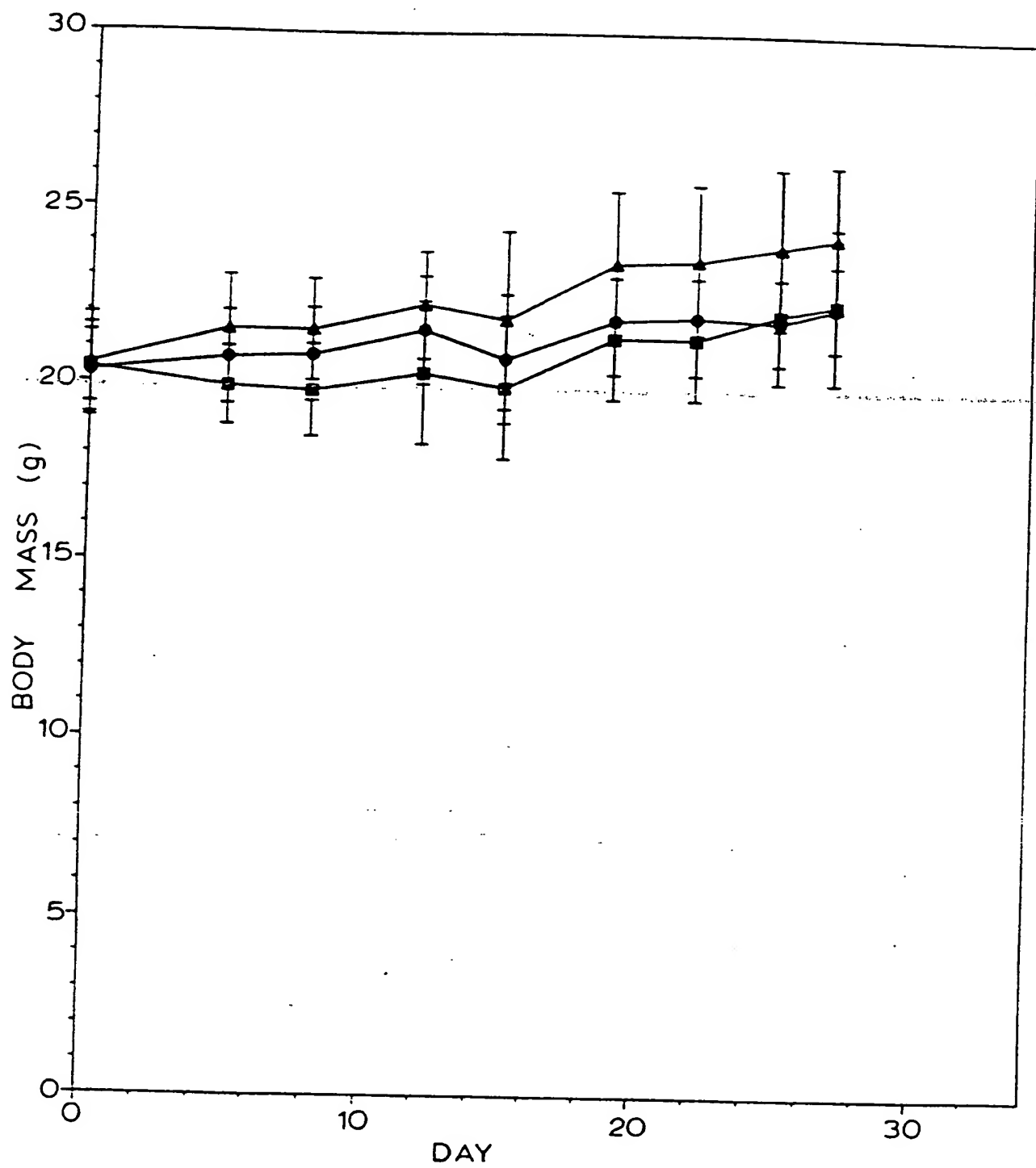


FIG.28F

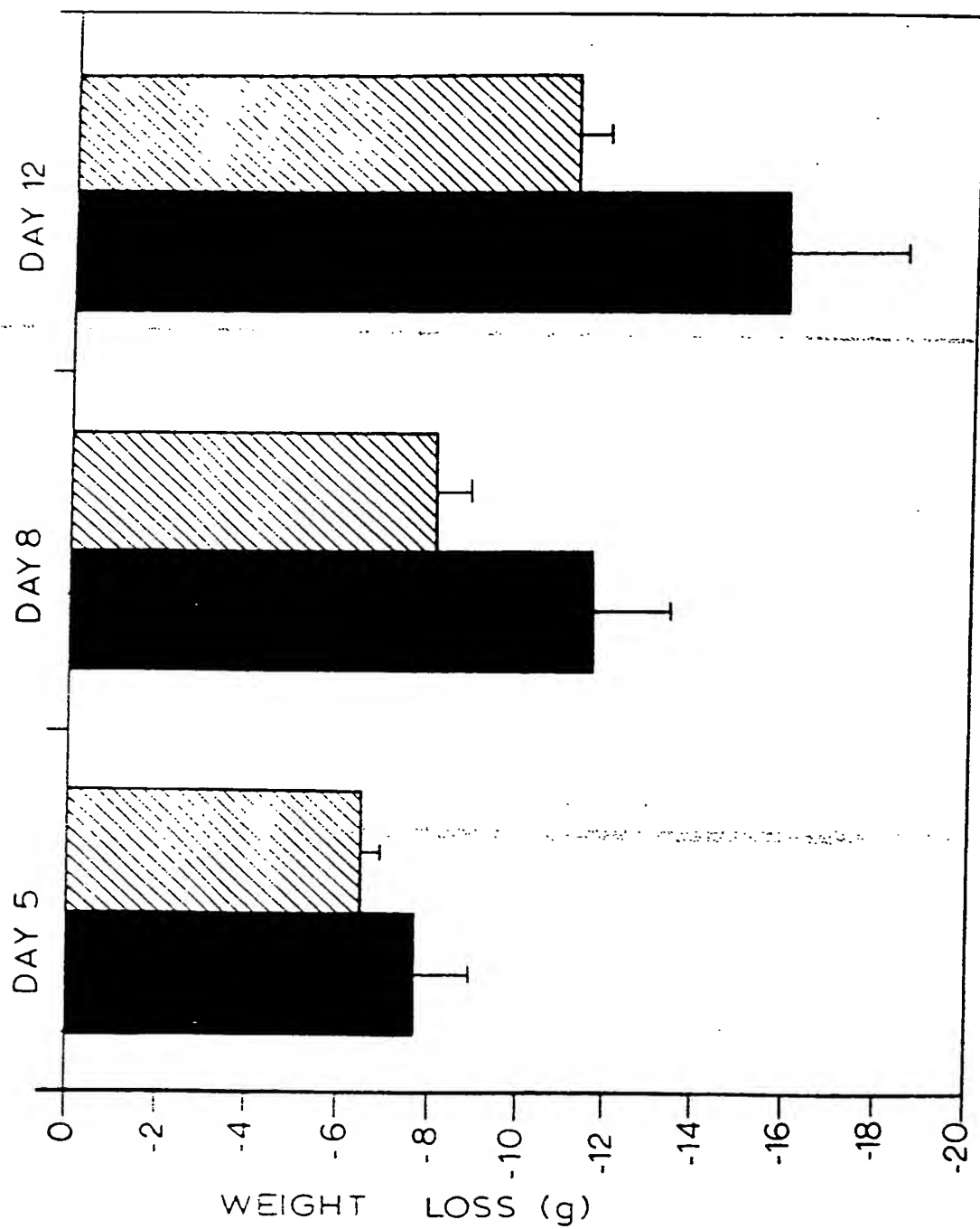


FIG. 29A

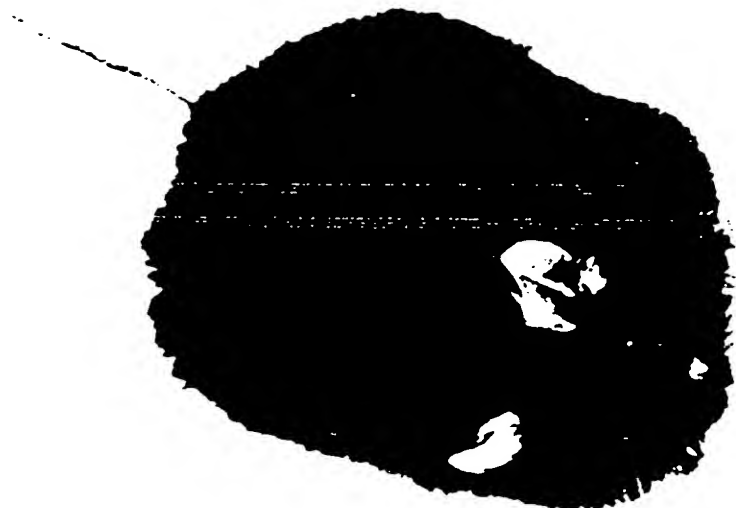


FIG. 29B



FIG.29C

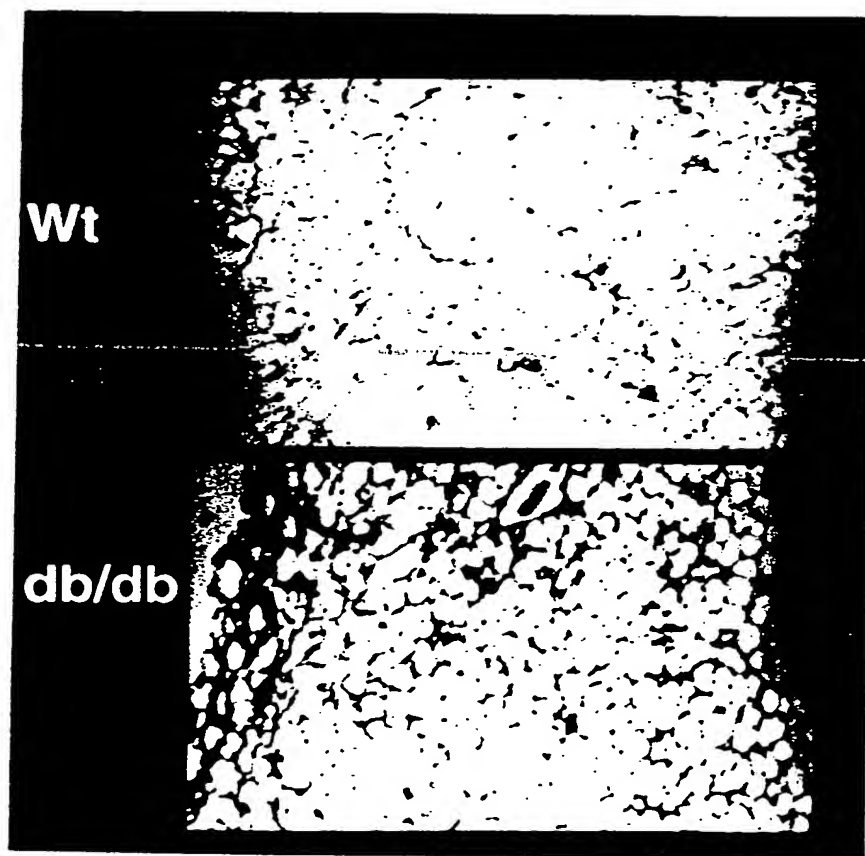


FIG.30

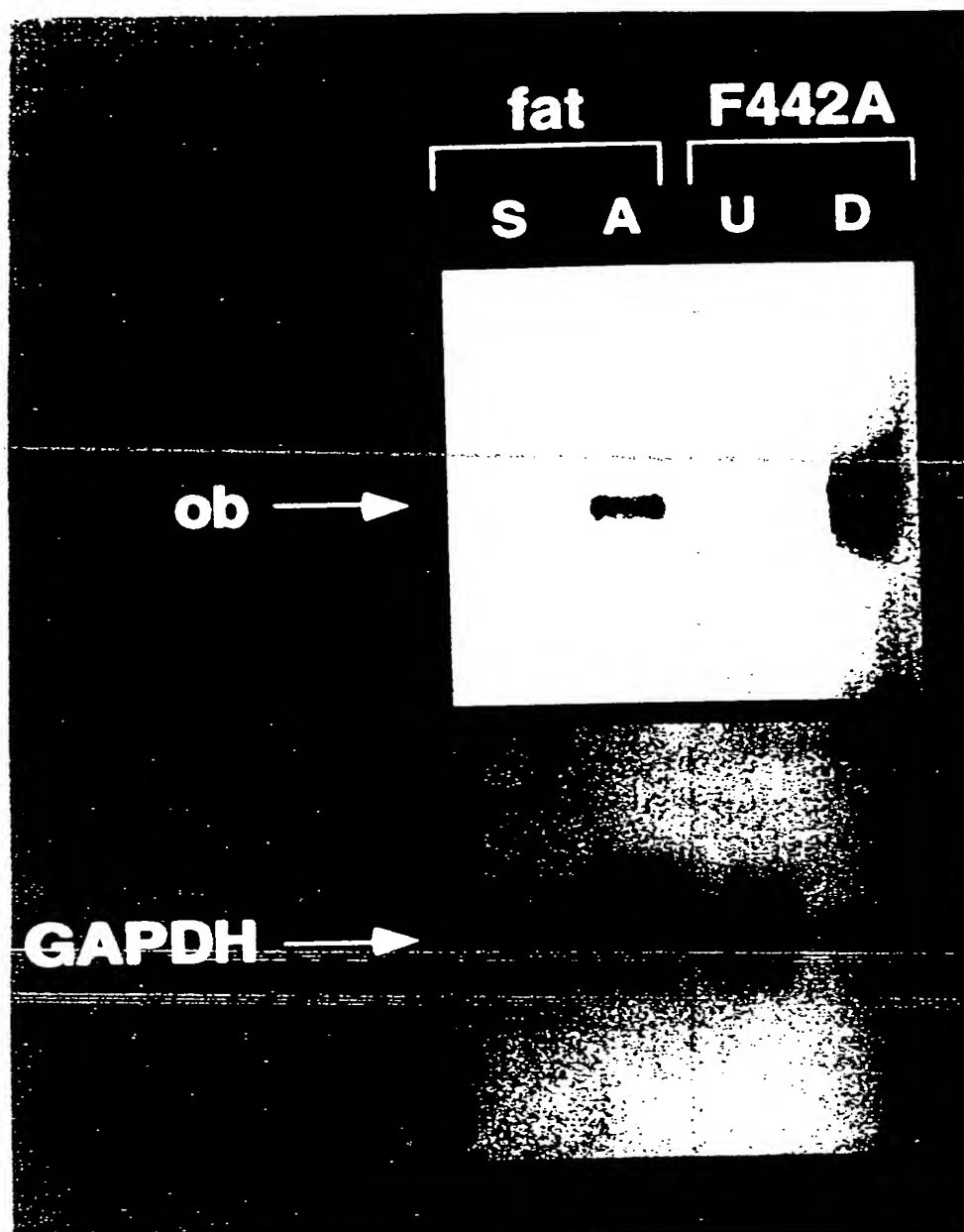


FIG.31

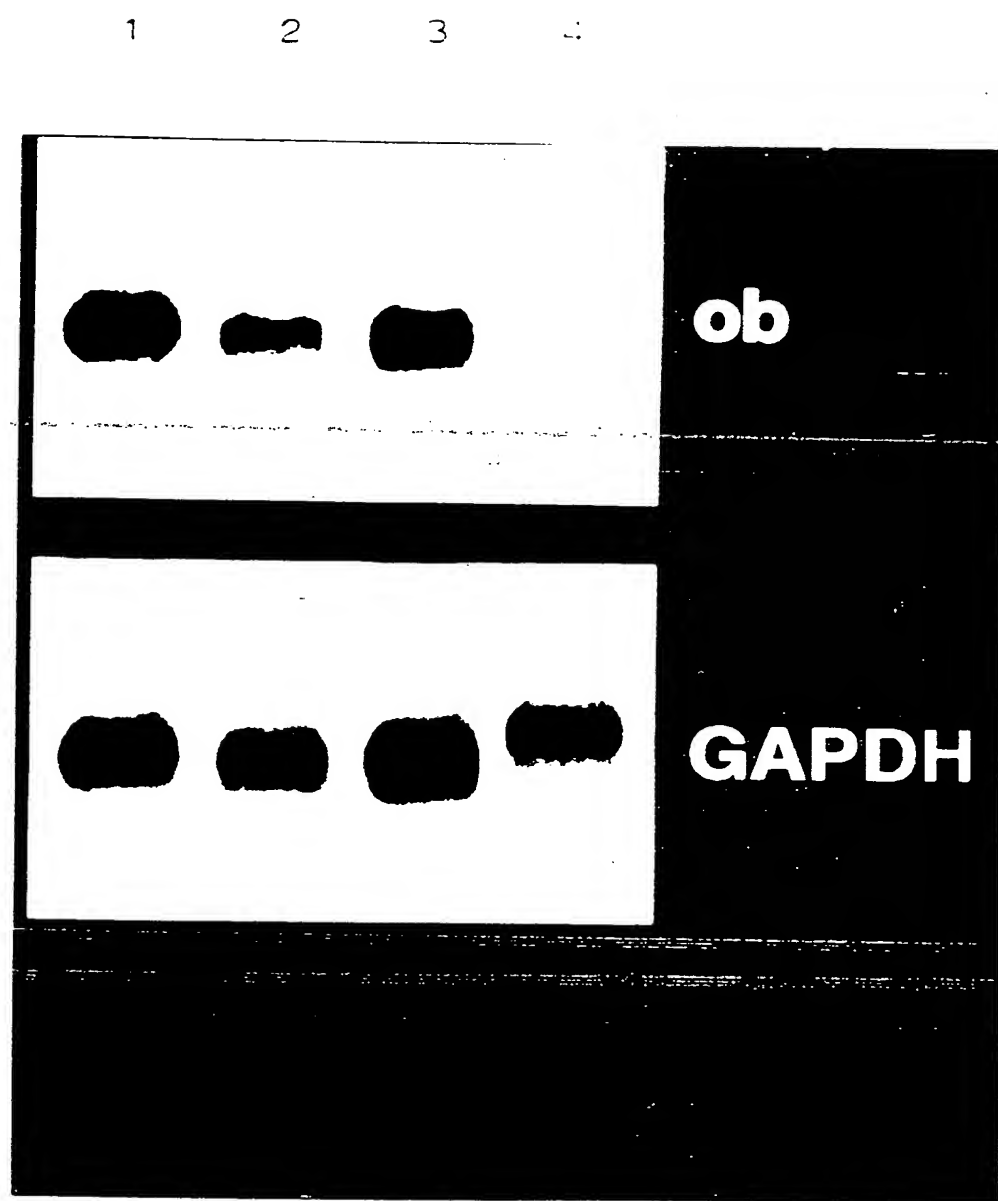


FIG.32A

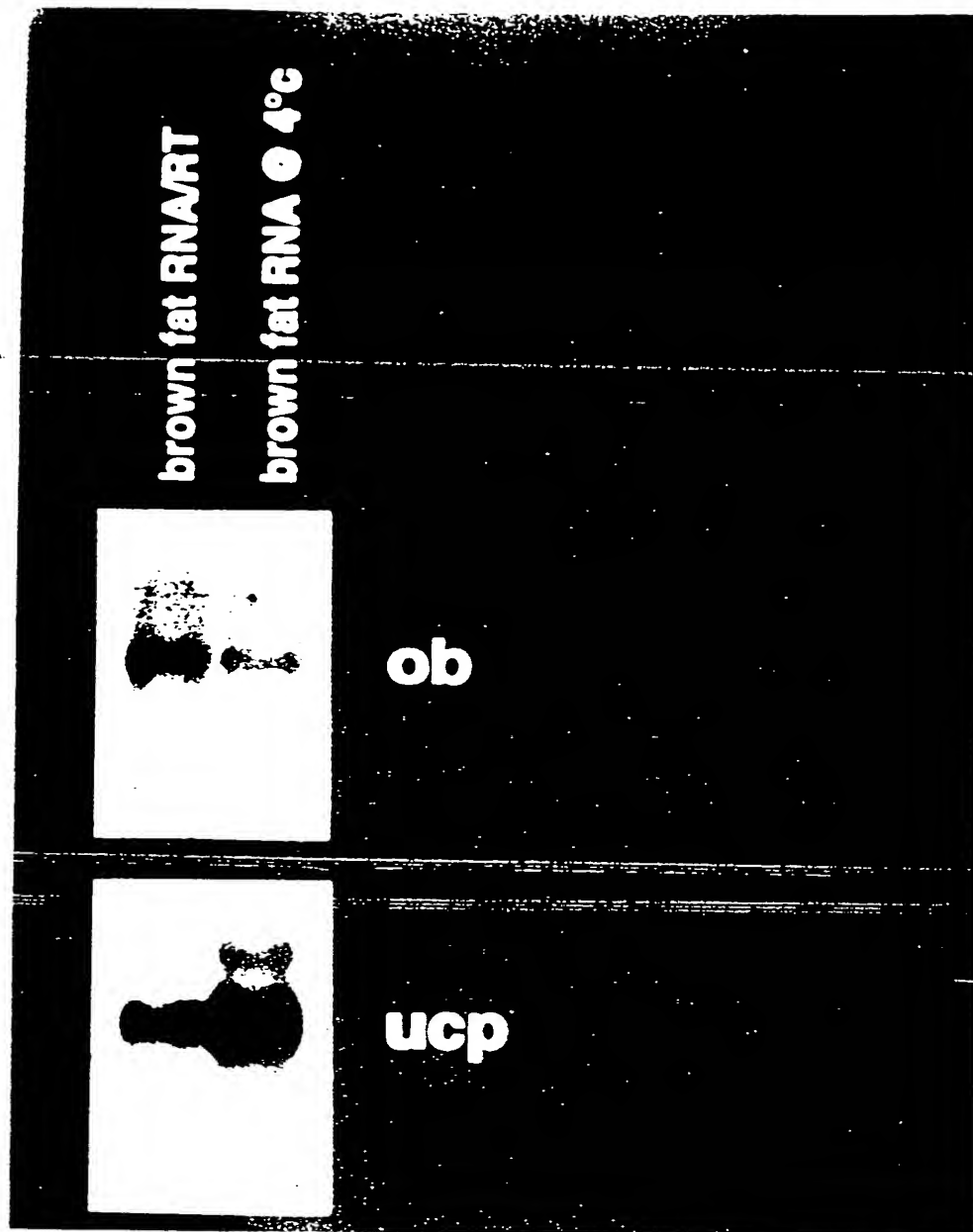


FIG.32B

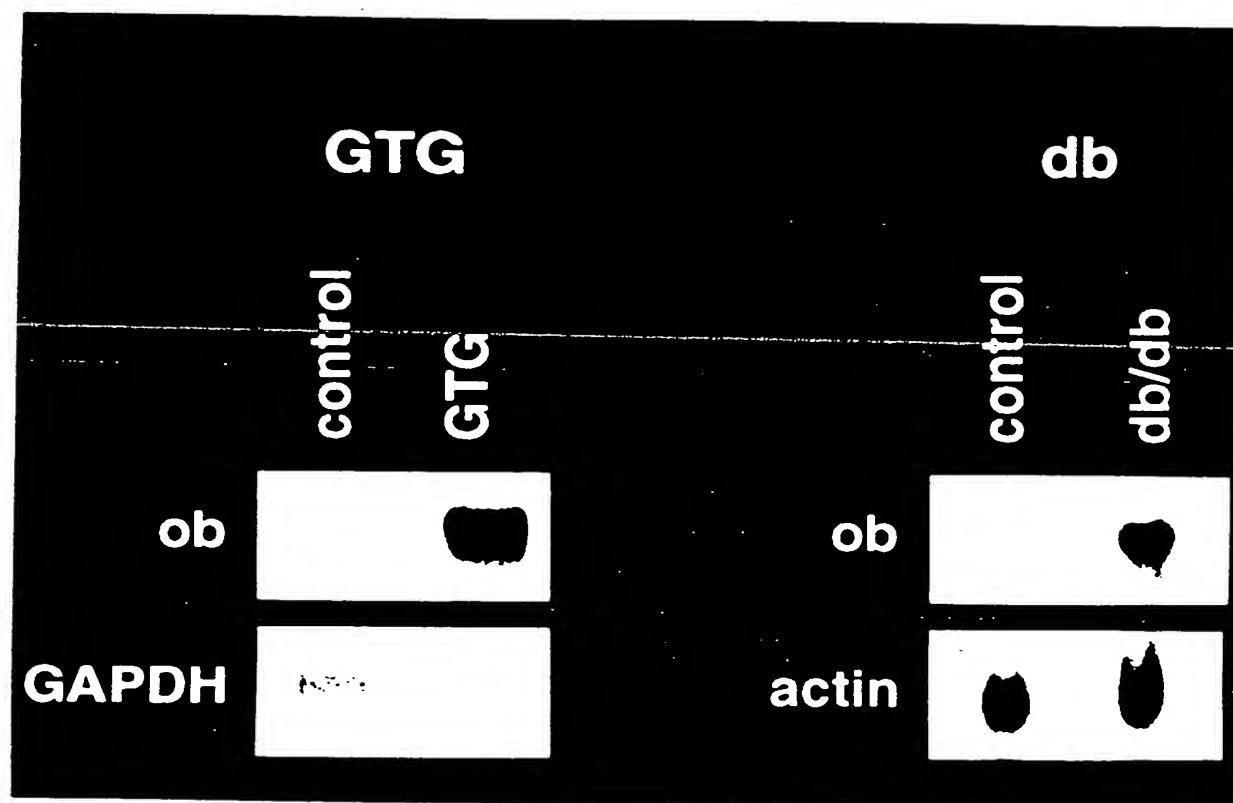


FIG.33

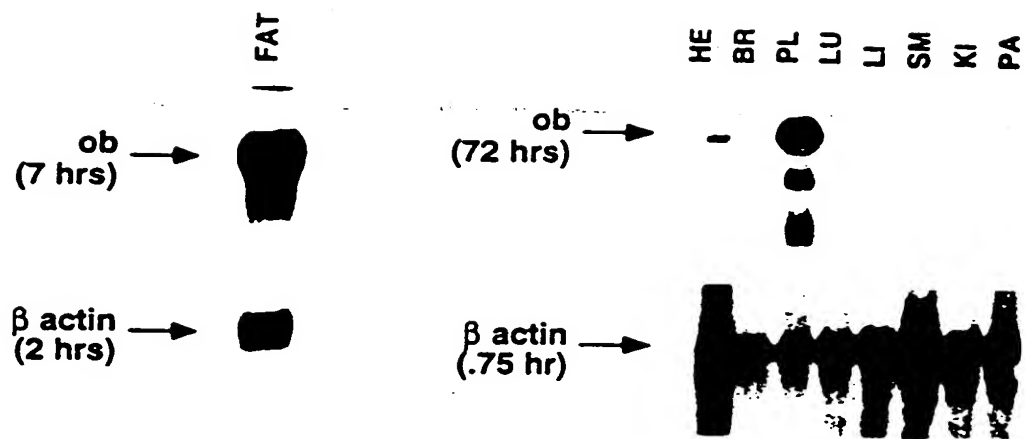


FIG.34

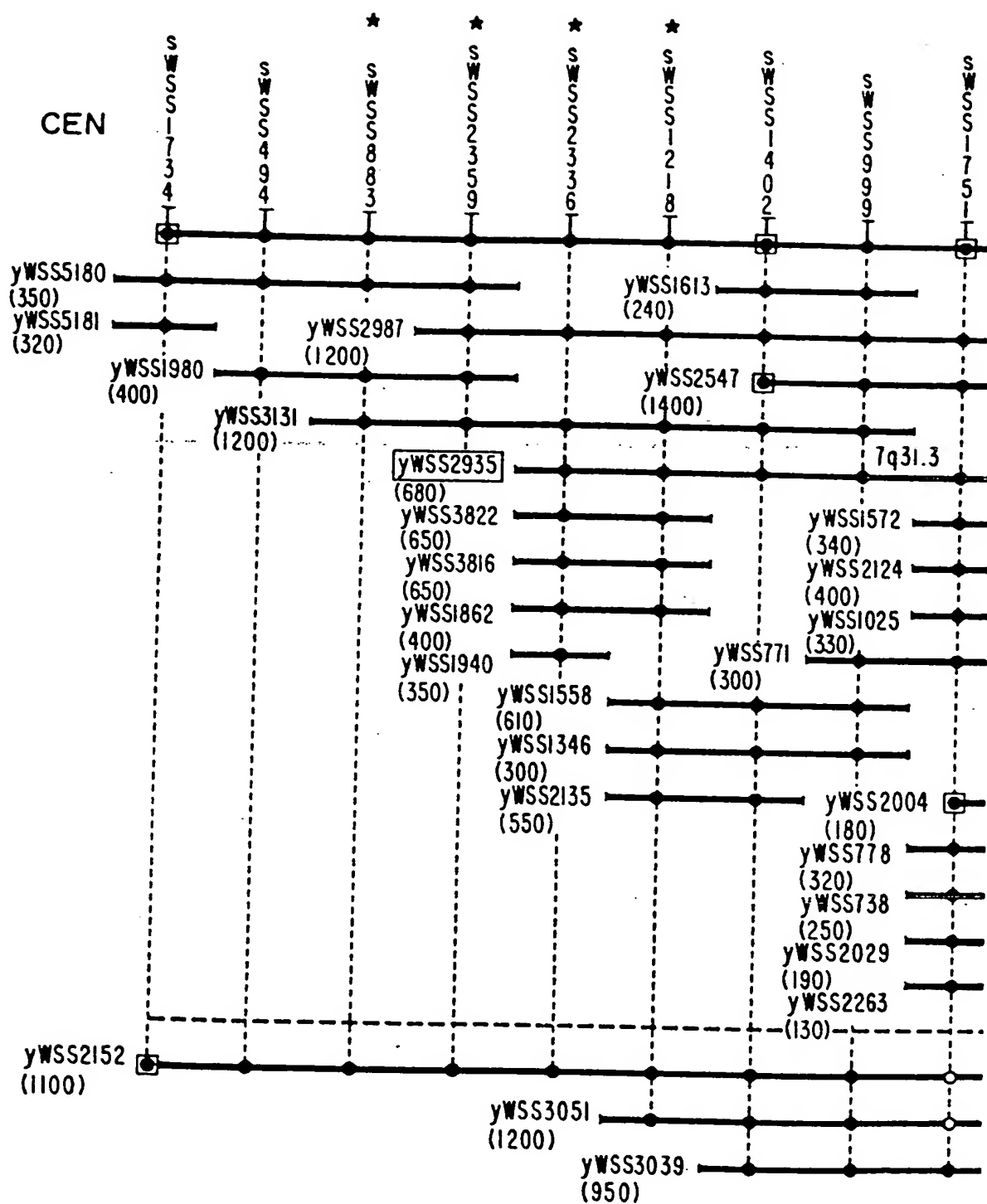


FIG. 35A

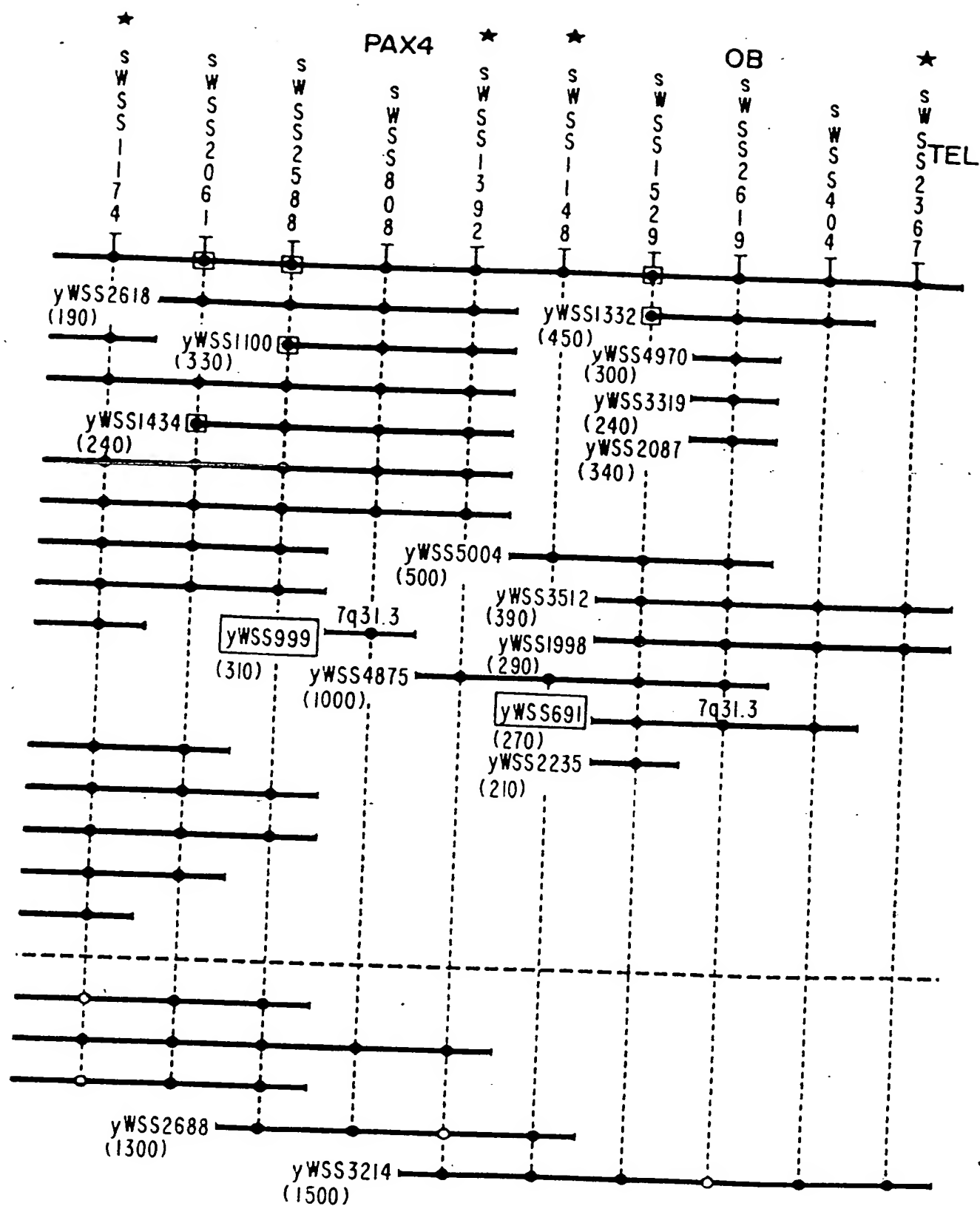


FIG. 35B